IN THE UNITED STATES DISTRICT COURT

IN AND FOR THE DISTRICT OF DELAWARE

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SHIRE DEVELOPMENT INC., SHIRE PHARMACEUTICAL DEVELOPMENT, INC., COSMO TECHNOLOGIES LIMITED, and GIULIANI INTERNATIONAL LIMITED,	:	CIVIL ACTION
Plaintiffs,	:	
v	:	
CADILA HEALTHCARE LIMITED (d/b/a ZYDUS CADIL) and ZYDUS PHARMACEUTICALS (USA) INC.,	:	
Defendants.	:	NO. 10-581-KAJ

- - -

Wilmington, Delaware
Wednesday, March 30, 2016
Bench Trial - Volume C

- - -

BEFORE: HONORABLE **KENT A. JORDAN**, U.S.C.C.J.

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P R O C E E D I N G S

(REPORTER'S NOTE: The following bench trial proceedings were held in open court, beginning at 9:00a.m.)

THE COURT: Good morning.

(Counsel respond, "Good morning, Your Honor.")

THE COURT: Let's be seated. All right.

Mr. Gaertner?

MR. GAERTNER: Good morning, Your Honor. Mike Gaertner.

We're going to start off the morning by playing some deposition testimony, and if I could, I'd like to introduce my colleague, Wasim Bleibel.

THE COURT: What's the gentleman's name again?

MR. GAERTNER: Wasim.

THE COURT: How do you spell that.

MR. GAERTNER: B-l-e-i-b-e-l.

THE COURT: Bleibel. Okay.

MR. GAERTNER: Yes, sir.

THE COURT: All right.

MR. GAERTNER: Thank you.

THE COURT: Thank you.

MR. BLEIBEL: Good morning, Your Honor.

THE COURT: Good morning, Mr. Bleibel.

MR. BLEIBEL: My name is Wasim Bleibel, and this morning we're going to play for you the deposition designations through video of Massimo Pedrani, and I can spell that, P-e-d-r-a-n-i, Luigi Moro, M-o-r-o, Srini Tenjarla, S-r-i-n-i T-e-n-j-a-r-l-a, Kiran Hothur, H-o-t-h-u-r, first name, K-i-r-a-n.

And before we run the videos, the parties discussed whether or not it would be necessary to designate the portions of the testimony that identified the particular 30(b)(6) topics that a witness may be designated, designated on, and the parties agree that it would not be necessary unless there's some sort of disagreement.

And the witnesses we're presenting today, we do not believe there are any disagreements about their designation, 30(b)(6) witness on the particular topics I will read to you. And so with that, I will just, if I have the Court's permission, introduce the witnesses with a brief summary of who they are and what topics they're designated on.

THE COURT: Fine. Are these videotape?

MR. GAERTNER: These are videotape. I also have binders with the clip reports for you to follow along. The videos will have streaming text and the exhibits.

THE COURT: All right. Having the marked transcript will be a help though. Thank you.

MR. BLEIBEL: Of course. May I approach the bench?

THE COURT: Please.

(Binders handed to the Court.)

THE COURT: You may proceed.

MR. BLEIBEL: Your Honor, the first witnessed that the defense calls to the stand through a video designation is Massimo Pedrani.

Mr. Pedrani was identified as a 30(b)(6) witness for Cosmo Technologies Limited on the following topics. The function of each excipient, including, but not limited to, the effective, the effect of each excipient on the solubility or release of mesalamine in 1.2 gram delayed release mesalamine tablet.

THE COURT: All right. He's a 30(b)(6) witness for what entity?

MR. BLEIBEL: This would be for Cosmo Technologies Limited. And, further, he was identified as a 30(b)(6) witness on the function and use of magnesium stearate in any pharmaceutical product manufactured or sold by Cosmo.

THE COURT: All right. Thanks.

(The videotaped deposition of Massimo Pedrani was played as follows.)

"Question: Can you please state your:

Question: Mr. Pedrani, can you please state your full name for the record?

"Answer: My name is Massimo Pedrani.

"Question: And during the period from 1997 through 2001, did you do any work as a consultant for Cosmo pharmaceuticals?

"Answer: Yes, sir.

"I was a consultant of the company since the beginning, from the foundation of the company.

"Question: Your name is shown on the face page of the patents as one of the inventors, is that correct?

"Answer: My name is included in the inventor, yes.

"Question: You mentioned earlier about something being old.

"Are matrix systems, systems that have been known for a long time in the pharmaceutical industry?

"Answer: I say that in the matrix system is well-known in the pharmaceutical field, working to control, modify or slow the release. When I say old, well-known. Better to say is well-known.

"Question: Other than the magnesium stearate, what other excipients are well-known to have lubricant properties?

"Answer: There are other products like magnesium stearate, all the stearic acid derivative, stearic fumarate.

"Question: Do you need a lubricant in order to make an acceptable product?

"Answer: Yes, to my knowledge.

"Question: In order to determine which specific excipient in a drug product is performing the function of slowing the release or retarding the release of the active ingredient in a dissolution test, would you need to conduct multiple tests with different quantities of the excipient of interest?

"Answer: That's my recommendation, to see quality of an excipient and the quantity.

"Of course coming back to physical properties, we know that you have different cellulose, under the general name of cellulose, but in the same paragraph there are cellulose that can have different physical properties, that's different viscosity, so the viscosity is something that you can measure easily.

"Question: What type of test would you do to determine whether or not magnesium stearate was capable of forming a matrix?

"Answer: Well, we have to substitute our lipophilic to put magnesium stearate in the first part of

the process, together with the process in the beginning to create the inert matrix to see if it is working in the way as well as stearic acid or carnauba wax or together.

"Question: How would you measure or what test would you employ to measure whether it was working in a way such as stearic acid or some other wax, what test would you employ?

"Answer: I think that we have to repeat the formula with magnesium stearate and inside, in the matrix, to see if we have the same dissolution profile controlling the release as well as the carnauba wax and stearic acid did together with hydrophilic matrix.

"Question: How would you know it was not some other excipient that was providing the change in dissolution that you are observing?

"Answer: Because in the last five, six years we did a lot of work with different demonstrative influence with inert matrix alone, with hydrophilic, without hydrophilic and hydrophilic alone and we saw some difference in the dissolution profile.

"Question: Did you have any discussions with anyone about what the '248 patent taught or described, because there is a difference between, as you say it, there is a difference between what's set forth in the developmental report and what's actually in the patent,

because the developmental report says the concept is porization and the patent says the same notation of canalization.

"Did you have any discussions with anyone about that?

"Answer: No, I don't remember. I think, you know, English not our mother tongue, so we some time have difficulty.

"Question: Does canalization allow for linear release of the active ingredient of a tablet?

"Answer: Canalization is a way how the API can go through when the system is in contact with biological fluid.

"Question: Is it a linear release?

"Answer: Linear release, yes.

"Question: In the '248 patent, which you still have I think in front of you, Defendants' Exhibit No. 109, was a hydrophilic polymer mixed in the substances that formed in the inert matrix?

"Answer: Yes, seems to be."

(End of videotaped deposition.)

THE COURT: Can I just interrupt to ask, the reference was being made to the '248 patent. Does somebody want to, do the parties have a -- I take it that that is different from the '720 patent? What patent was that

about?

MR. PETERKA: Good morning, Your Honor. Jim Peterka for defendant.

The '248 patent is actually, it's a patent that's described in the background section of the '720 patent. It's at column 1, starting at line 48 through 52 and it reads, the same note, describing a prior art formulation saying, the same notion of canalization of inert matrix is described in U.S. Patent No. 4,608,248, in which a small amount of hydrophilic polymer is mixed with the substances forming an inert matrix in a none sequential penetration of different matrix materials.

THE COURT: Okay. I got it. Thanks.

MR. PETERKA: Thank you.

THE COURT: All right. Mr. Bleibel, do you have any exhibits associated with this deposition that are to be offered in evidence?

MR. BLEIBEL: We do. DTX-1, I believe, is already in evidence as PTX-1, which is the '720 patent, so the exhibit I offer into evidence at this time is DTX-156, which is U.S. Patent No. 4,608,248.

THE COURT: Okay.

MR. HAUG: No objection, Your Honor.

THE COURT: All right. Admitted without objection.

(DTX-156 was admitted into evidence.)

THE COURT: Your next witness?

MR. BLEIBEL: Thank you, Your Honor.

The defense at this time now calls to the stand by video deposition designation Luigi Moro, who at the time of his deposition was a chief scientific officer at Cosmo Pharmaceutical and Cosmo Technologies, and was identified as a 30(b)(6) witness for Cosmo Technologies on the following topics. Any research, development, or manufacturing related to 1.2 grams delayed relief mesalamine tablets, including but not limited to the identity and role of the individuals involved in the formulation, manufacturing and testing of the 1.2 gram delayed release mesalamine tablet and the conduct and result of all bioavailability studies of 1.2 gram delayed release mesalamine tablet.

I also have some binders for you.

THE COURT: Please.

MR. BLEIBEL: May I approach the bench?

THE COURT: Yes.

(Mr. Bleibel handed binders to the Court.)

(The videotaped deposition of Luigi Moro was played as follows.)

"Question: Mr. Moro, can you state your full name for the record.

"Answer: My full name is Luigi Moro.

"Question: What is your current title or position?

"Answer: I am the chief scientific officer in Cosmo Pharmaceutical and Cosmo Technologies.

"Question: Have you ever discussed with anyone in your entire career in the pharmaceutical industry the use of magnesium stearate in any functional role other than as a lubricant?

A. I don't discuss, but I read paper when magnesium stearate in some cases has been used as hydrophobic agent.

Q. Have you ever used magnesium stearate as a matrix-forming material?

A. The answer is no.

Q. How long before 1999 did you know that polymers can form matrices?

A. I attended a class on controlled release technologies in the beginning of the year '80, I don't remember exactly when.

Q. What year was that?

A. 1980, when they were teaching, teacher taught me the meaning of controlled release mechanism and structure.

Q. You mentioned the word structure; what structure do excipients that have controlled release capabilities or are capable of controlling release, what types of structures do they have?

A. What I mean structure is not referring to the single excipient or a single component, but structure is a term referring to the formulation. And I told you before, reservoir is a type of structure and matrix is another type of structure.

Q. I have had marked as deposition exhibit number DDX 103 a document bearing Bates stamp number COMESA 0006353 through 6384. I would ask you if you can identify this document?

A. Yes, it looks like a presentation of 5-ASA formulation on the market, delivery characteristics and distribution into the gut.

Q. Have you seen this document before?

A. Yes.

Q. When did you first see this document, if you can recall, and I realize it has been a long time?

A. I remember that this document is a presentation that Giancarlo Naccari, I don't remember in what kind of meeting or symposium, and he showed me this document when he prepared.

Q. Do you recall approximately what year that was?

A. I don't recall exactly, maybe two, three years ago, but I am not sure about it.

Q. Showing you what has been marked as Defendants' Exhibit Number 110. Can you identify this document for the record, Mr. Moro?

A. It is a presentation that is belonging in a meeting, maybe manufacturing committee, and there are represented several descriptions, specs and activity done for the project.

Q. I would like you to turn now to page 5570 and the heading of this particular document says, "Mesalamine 1,200 milligram MMX tablets first level change proposed formula," do you see that?

A. Yes.

Q. And in the description, the vertical column, there is a list of ingredients, one of which is magnesium stearate. Do you see that?

A. Yes.

Q. It says that the current formulation is 14 milligrams per unit and the formula with first level change is to be 11 milligrams per unit. Do you see that?

A. Yes.

Q. And the amount of percentage variation for that three milligram reduction in magnesium stearate is .23 percent; is that correct?

A. That's correct.

Q. And right below that it has a parenthesis that says, "lim .25 percent plus or minus 3.305 milligram," do you see that?

A. Yes.

Q. Do you know what that reference is with respect to?
A. The number in parentheses are the specs range, specification range.
Q. When you say specification range, what do you mean by that?
A. I mean the limit in which this variation is tolerated as actual.
MR. PARR: I would like to mark as DDX 111 this document, which has a heading, "Guidance for industry SUPAC-MR: Modified release solid oral dosage forms."
First, Mr. Moro, can you identify this document for the record; I identified it briefly, but if you could more thoroughly identify what it is.
A. It is a guidance for industry called SUPAC modified release solid oral dosage form, guidance that belonged to the FDA guidance, books and collection, addressing the work of the people that are in control of this development field.
Q. Have you seen this guidance before my showing it to you?
A. Sure.
Q. I would like you to turn your attention to page three of this guidance and under A where it says "level one change," do you see that heading, first of all, A, level one change?
A. Yes.

Q. And actually the heading above it, over on page two, Roman numeral number three, says "components and composition, nonrelease controlling excipient; do you see that?

A. Yes.

Q. Going back to page three, under the heading level one change, it defines level one changes as, "Changes that are unlikely to have any detectable impact on formulation quality and performance."

Do you see that?

A. Yes.

Q. And performance would include dissolution or release of the drug, wouldn't it?

A. Sure.

Q. Let's go back to the slide presentation that we were looking at before, COMESA 0005570 is the specific page?

A. Yes.

Q. I would like again to refer you to that limit of 0.25 percent; is that the same limit that is shown in the FDA's guidance?

A. I think so.

Q. Turning to page 5572 of the slide presentation, the information that is shown on this page is taken directly from the FDA's guidance; correct?

A. Yes.

(End of videotape.)

MR. BLEIBEL: That's the conclusion of Luigi Moro's testimony. At this time, defense would move into evidence DTX 21, DTX 22, and DTX 183.

MR. HAUG: No objection.

THE COURT: All right. They're admitted without objection. Next witness.

MR. BLEIBEL: Thank you, Your Honor.

The next witness by video deposition designation will be Srini Tenjarla. At the time the deposition was taken was senior director in the development of pharmaceutical sciences as Shire Pharmaceuticals and was designated as a 30(b)(6) witness for Shire Development and Shire Pharmaceutical Development, Inc. on the following topics: The formulation and manufacturing process for 1.2 grams delayed release mesalamine tablets; the function of each excipient including but not limited to the effect of each excipient on the solubility and/or release of mesalamine in 1.2 gram delayed release mesalamine tablets; the function and use of magnesium stearate to form a matrix in any pharmaceutical product manufactured and sold by Shire; and any study or analysis of magnesium stearate as matrix forming agent.

THE COURT: Before we start, how would you offer the technology part? I just got a question for you. Why

was Cosmo a 30(b)(6) witness? Who wants to speak to that?

MR. PETERKA: Good morning, Your Honor. The inventors of the patent were Cosmo employees and they were the patent holder.

THE COURT: Sure, I understand that the inventors are the inventors, I'm talking about Cosmo as a witness.

MR. PETERKA: They're the patent holder.

THE COURT: They are the assignee of the patent?

MR. PETERKA: Yes.

THE COURT: Good enough.

MR. PETERKA: Sorry I neglected that. The plaintiffs are Shire, Cosmo, it was Giuliani, now it's Nogra, they were the involved entity.

THE COURT: Okay.

MR. BLEIBEL: I have some binders for you as well. May I approach the bench?

THE COURT: Yes.

(Videotape deposition.)

"Question: Can you state your name for the record?

"Answer: My name is Srini Tenjarla.

"Question: Who is your current employer?

"Answer: Shire Pharmaceuticals.

"Question: What is your current title?

"Answer: I am a senior director in the department of pharmaceutical sciences.

"Question: When did you obtain your Ph.D.?

"Answer: 1989.

"Question: What was your Ph.D. in?

"Answer: In pharmaceutical formulations.

"Question: How long were you a professor at Mercer?

"Answer: Approximately from 1990 to 1997.

"Question: When you were a professor, generally what types of courses did you teach?

"Answer: Pharmaceutics. Pharmacokinetics.

"Question: You're familiar with Lialda; correct?

"Answer: Yes, I am.

"Question: Do you understand what I mean if I refer to it as SPD476?

"Answer: Yes, I do.

"Question: You said the terminology as far as the SPD476 is concerned, we call it lipophilic. What do you call lipophilic?

"Answer: The excipients, the lipophilic excipients in the product.

"Question: Which excipients are those?

"Answer: Those would be stearic acid and the

carnauba wax.

"Question: Is that it?

"Answer: Yes, to my knowledge.

"Question: I am going to hand you what's previously been marked as DDX 113. I want you to take a look at the document and just let me know if you recognize it?

"Answer: Yes, I do.

"Question: What is this document?

"Answer: It is something called the quality overall summary and it's part of the NDA submitted by Shire to the FDA.

"Question: What was your involvement in the preparation of the NDA?

"Answer: I was involved in the preparation of the module three and the quality overall summary.

"Question: Is magnesium stearate a well-known lubricant?

"Answer: To my knowledge, magnesium stearate is a lubricant.

"Question: Does it perform any other function in the SPD476 product?

"Answer: In SPD476 it is used as a lubricant.

"Question: It is used as a lubricant only, is that right?

"Answer: To my knowledge, yes.

"Question: Do you know of any other properties of magnesium stearate?

"Answer: Not to the best of my knowledge, no.

"Question: Are you aware of any pharmaceutical formulation in which magnesium stearate is used as anything other than a lubricant?

"Answer: No, I do not.

"Question: To your knowledge, there are no products that use magnesium stearate to form a matrix; is that correct?

"Answer: Yes, that is correct.

MR. PETERKA: I am going to ask to be marked as Exhibit 161, DDX 161, this is a document, an E-mail and attachment, and the whole range is PLMESA 959749 through 959789.

"Question: And the document that's attached to this E-mail, which starts at page 99752, can you describe this document?

"Answer: It is called a briefing document; it is submitted to the FDA prior to the actual meeting.

"What I do not know right now is if this is the final draft that was submitted or it was a previous draft.

"Question: Do you have any reason to doubt that

this was the final draft?

"Answer: Looking at the content, I would probably say it pretty close to the final draft, but I just cannot say for certain.

"Question: Does magnesium stearate have any effect on the dissolution profile of the SPD 476 product?

"Answer: To my knowledge, no.

"Question: Does magnesium stearate affect the release of mesalamine from the SPD 476 product?

"Answer: I do not believe so.

"Question: Did you draft this document that's attached, DDX-118?

"Answer: Yes, I believe so."

THE COURT: Hold on. Can you put up the document? If I don't have a copy of the transcript, I can't look around on it, so I need you to roll back there.

He refers to a, I'm assuming it's a chemical formulation by SPD, whatever it is. Can somebody tell me whether he identified what that thing is? I will expect somebody to pop up if they want to and make sure everybody agreed on it. I mean, I realize your lawyers' statements aren't evidence, but I'm looking for some help. What is it that he refers to it as?

MR. BLEIBEL: Sure. So at page 26, line 20, attorney Peterka asks: "You're familiar with Lialda;

correct?"

And the answer is: "Yes, I am."

"Question: And do you understand what I mean if I refer to it as SPD 476?

"Answer: Yes, I do.

THE COURT: All right. Thanks. That's all I need.

MR. BLEIBEL: This is an internal project code that they used to identify the product.

THE COURT: Good enough. Thank you. Thanks very much.

Go ahead and roll it.

"Answer: Yes, I believe so.

"Question: If you could turn to Page 2166 of this presentation, there is a table there, Asacol and Mesavant.

"Do you see that?

"Answer: Yes.

"Question: And this identifies Asacol as having an immediate release core, is that correct?

"Answer: Yes.

"Question: Is that your understanding of Asacol?

"Answer: Yes.

"Question: I am going to show you what's been

previously marked as DDX-117. It is an e-mail and attachment bearing Bates numbers COMESA 3747 through 3749.

"Still looking at DDX-117, there is a Table 1 in the attachment that says, 'Excipients contained in different mesalamine formulations in the USA/EU.'

"Do you see that table?

"Answer: Yes.

"Question: This table identifies Asacol as having magnesium stearate in the core. Is that accurate?

"Answer: Yes."

(End of videotaped deposition.)

MR. BLEIBEL: That's the conclusion of Mr. Tenjarla'S deposition designations.

THE COURT: All right.

MR. BLEIBEL: At this time defense would move into evidence DTX-153, DTX-173, DTX-44, and DTX-6.

(Pause while counsel conferred.)

MR. HAUG: No objection, Your Honor.

THE COURT: Okay. They're admitted without objection.

(DTX-153, DTX-173, DTX-44 and DTX-6 were admitted into evidence.)

MR. BLEIBEL: Thank you.

We have one last for this morning, Your Honor, and that would be Kiran Hothur.

He will be presented -- and at the time that the deposition was taken, he was a senior scientist with Zydus.

Mr. Hothur was designated to testify as a 30(b)(6) witness on the experiments and studies referenced in the Zydus product development report and the authentication of the lab notebook and experiments conducted by defendants in the development of the proposed ANDA product.

THE COURT: All right.

MR. BLEIBEL: I have binders.

THE COURT: Thank you.

MR. BLEIBEL: May I approach the bench?

THE COURT: Please.

(Mr. Bleibel handed binders to the Court.)

THE COURT: Before we -- how long is this clip going to take? Do you know?

MR. BLEIBEL: There clip will run six minutes, 59 seconds.

THE COURT: All right.

(The videotaped deposition of Kiran Hothur was played as follows.)

"Question: When did you get your Master of Pharmacy?

"Answer: I completed it in 2003.

"Question: Did you obtain an undergraduate degree?

"Answer: Yes.

"Question: And what was your undergraduate degree?

"Answer: Bachelor of Pharmacy.

"Question: Do you know who drafted the PDR or the Product Development Report that we marked as Exhibit 8?

"Answer: It was drafted by me.

"Mr. Walters: Did you prepare the text that's underneath 6.2 heading and continuing to the next page?

"Answer: Yes.

"Mr. Walters: This paragraph lists bulk density of the drug substance in the drug product as a desirable final product quality; is that accurate?

"Answer: Yes.

"Mr. Walters: Okay. Going to the first excipient that's listed here, carboxymethyl cellulose sodium, do you understand that to be an excipient exhibiting hydrophilic characteristics?

"Answer: Yes.

"Mr. Walters: And how about hypromellose, item number two here, do you know whether that excipient exhibits hydrophilic characteristics?

"Answer: Hydrophilic, yes.

"Mr. Walters: And how about magnesium stearate? Do you consider magnesium stearate to be hydrophilic or hydrophobic?

"Answer: Hydrophobic.

"Mr. Walters: What is your understanding of hydrophobic?

"Answer: It is water repellent.

"Mr. Walters: So it resists water?

"Answer: Yes.

"Mr. Walters: Based on your understanding of lipophilic properties, do lipophilic substances, in your understanding of those substances and their mechanics through your experience, do they also repel water or resist water?

"Answer: Yes, I think so.

"Question: Does this flow chart describe in general the steps in the manufacturing process that Cadila uses for its compacted API that is used in 1.2 gram mesalamine tablet?

"Answer: Yes.

"Question: Did you conduct trial batch FO27?

"Answer: Yes.

"Question: And based on the objective here, this experiment FO27 was done to roll-compact API and use in

formulation to improve bulk density and achieve target fill waits; is that right?

"Answer: Yes.

"Question: And the initial bulk density in this experiment was 0.18 grams per milliliter?

"Answer: Yes.

"Question: In your first trial, trial number one, the API was fluffy and flakes formed that were brittle without any strength; is that right?

"Answer: Yes.

"Question: And in your second trial, the API was roll-compacted again and you noticed that it improved the strength of the flakes; is that right?

"Answer: Yes.

"Question: It appears that bulk density at this trial, trial number 2, was 0.29 grams per milliliter?

Answer: Yes.

"Question: In your third trial, you noticed that the flow improved; is that right?

"Answer: Yes.

"Question: For the third trial, the API was roll-compacted again and you received a bulk density of 0.32 grams per milliliter; is that right?

"Answer: Yes.

"Question: And was there a fourth trial?

"Answer: Yes.

"Question: And for this fourth trial, the API was roll-compacted; is that right?

"Answer: Yes.

"Question: And you noticed a bulk density of 0.38 grams per milliliter?

"Answer: Yes.

"Question: Then you noted here in your observations that: The API was sticking on the rollers so lubricant addiction may improve the flow as well as compaction process?

"Answer: Yes.

"Question: What did you mean by that, compaction process?

"Answer: To make the process feasible and easy.

"Mr. Walters: Okay. Good. Let me ask the question again. Do you know whether this experiment FO27 is the first time that either you or Mr. Doss roll-compacted the API in a roll-compactor?

"Answer: Myself, I think. I think this is the first time.

"Question: And is that something that you came up with?

"Answer: Yes.

"Question: And did you also come up with the idea to roll-compact the API in a roll-compactor using magnesium stearate?

"Answer: Along with the colloidal silicone dioxide.

"Question: Okay. And for FO27 A, you noticed: 'No weight variation. No sticking or picking. Good flow properties. Good compactability. Target weight was achieved after improved bulk density.' Is that right?

"Answer: Yes.

"Question: Mr. Hothur, do you recognize what we marked as Exhibit 20?

"Answer: Yes.

"MR. WALTERS: Okay. Can you turn to the page that is marked 212133? Do you see that page?

"Answer: Yes.

"MR. WALTERS: Do you believe that Zydus' mesalamine tablet 1.2 gram is formulated with only a hydrophilic matrix?

"Answer: Yes.

"MR. WALTERS: And do you believe that Cadila's mesalamine DR tablet 1.2 gram avoids lipophilic matrix formers?

"Answer: Yes."

(End of videotaped deposition.)

THE COURT: All right.

MR. BLEIBEL: That's the conclusion of Mr. Hothur.

At this time, the defense would move into evidence DTX-24, PTX-205, and PTX-215.

MR. HAUG: No objection, Your Honor.

THE COURT: All right. Thank you. Thanks very much.

MR. BLEIBEL: Thank you, Your Honor.

(DTX-24, PTX-205, and PTX-215 were admitted into evidence.)

THE COURT: Mr. Gaertner and Mr. Haug, let's put this on the clock on me at this point. All right? I will ask the clerk not to charge this to Zydus.

I have a couple of questions, which I probably should have asked right at the beginning, but the videos prompted. You can answer now or think about how you want to answer. But I just would like to get a fix on the relationship of the parties. Okay?

I understand that Cosmo is -- I should have paid attention to it, I guess, the owner of the patent. I assume that they are, have assigned the patent to Shire for purposes of taking advantage of it here in the United States. I would be curious to know if it's an exclusive licensee in the U.S. Who is Giuliani International Limited?

Why are they a plaintiff? What is going on with them? Are they still active in the place? What's the relationship between Cadila and Zydus? They seem to be sister companies, but separate companies.

Sometimes you see the Cadila name. Sometimes you see the Zydus names. Sometimes you see Zydus and Cadila together.

You know, I'm embarrassed to be saying at the beginning of the third day of trial, I'm asking for this clarification. But does somebody want to tell me? Like give me a program so I know who the players are.

MR. GAERTNER: I will let Mr. Haug do the first part and I will do the second part, if you would like, Your Honor.

THE COURT: All right.

MR. HAUG: Well, Your Honor, Cosmo is the patentee. They have exclusively licensed the patent to what was Giuliani. Right? And is has now changed their name to Nogra, N-o-g-r-a Pharma Limited, which was, as I said, is the exclusive licensee of the '720 patent. And they in turn have granted an exclusive sublicense to Shire.

And this is all set forth in paragraph 10, actually, Your Honor, of the statement of uncontroverted facts.

THE COURT: Okay.

MR. HAUG: In the Pretrial Order.

THE COURT: All right.

MR. HAUG: So that's how Shire has the rights on these patents.

THE COURT: Perfect.

MR. HAUG: And we represent all of those parties.

THE COURT: All right. I knew it would be in here someplace. All right.

MR. GAERTNER: Good morning, Your Honor. Mike Gaertner.

I will answer the second part with respect to Cadila and Zydus.

Zydus Pharmaceuticals USA is the marketer of the product and the holder of the ANDA for the generic mesalamine 1.2 gram delayed release tablet that's at issue here. It's an affiliate of Cadila Healthcare, Incorporated, I'm sorry, Limited, which is in India. They are the manufacturer of the product.

THE COURT: All right. Okay. Perfect. Good enough. All right.

Now we're off my clock and we're back on the defendants' clock.

MR. GAERTNER: All right. Your Honor, the defendants would like to call as the next witness Dr. Robert

Bellantone.

THE COURT: All right.

... ROBERT A. BELLANTONE, having been duly sworn as a witness, was examined and testified as follows ...

THE COURT: Mr. Gaertner, do you have exhibits?

(Mr. Gaertner handed notebooks to the Court and to the witness.)

THE WITNESS: Thanks.

DIRECT EXAMINATION

BY MR. GAERTNER:

Q. Good morning, Dr. Bellantone. Would you please state your name and address for the record?

A. Yes. Robert A. Bellantone. 67 Davenport Road, Yonkers, New York.

Q. And what is your profession, Dr. Bellantone?

A. I'm a pharmaceutical scientist, recently retired as a professor from Long Island University.

Q. All right. Can we please put up slide 2.

Dr. Bellantone, before we get started here, could you briefly describe your educational background for the Court?

A. Yes. I earned a Bachelor's in pharmacy in 1976 from the University of Connecticut. Some year later I went back to school to study for a Ph.D. in pharmaceutical sciences.

I was in that field for several years, took all the courses, but some of the courses that I had taken along the way involved some physics and engineering, and I was very struck with those, so I changed my field of study and I obtained my Ph.D. in physics in 1992.

Q. And from where did you obtain your Ph.D.?

A. That was also from the University of Connecticut.

Q. Please describe your professional experience since obtaining your Ph.D.

A. Yes. Well, for the past 20 years I've been affiliated with Long Island University. I taught one graduate course as an adjunct in 1995 and I applied and received a full position in the fall of 1996.

I went through the associate, assistant associate and made a full professor, and I, as I said, I retired from there very recently, at the end of the fall of 2015 semester.

Q. Can you describe for the Court some of the courses that you taught while at Long Island University?

A. Yes. Well, since 2004, most of my teaching has been in the graduate program, especially Ph.D. courses. I have taught courses in drug delivery, controlled release, dosage form design, physical pharmacy and physical chemistry.

Q. Have you taught any courses that you believe are particularly relevant to the issues that you have been asked

to consider in this case?

A. Yes, one of my Ph.D. courses called interfacial phenomenon is a course in surface interaction and I believe that's very relevant to the case.

Q. Can you explain to the Court why you believe that experience is relevant?

A. Yes. Well, interactions that go on in interfaces are I think particularly applicable to this case, for instance, the interaction of water with excipients, or with API is very important, and the nature of those interactions and the strength of those interactions will have a profound affect, for instance, if water is in contact with a surface, and if they like each other the water will tend to spread and wet the surface, but if they don't like each other then the water will tend not to do that.

Q. Did you teach the courses on interfacial and surface chemistry to Ph.D. students at Long Island University?

A. Yes, I did. It turns out that in that course, we bring up a lot of concepts from math and physics and chemistry. And these are relevant to the pharmaceutical sciences, especially the origins of the interactions and so on, but it also turns out that's not an isolated event because a lot of things that go into pharmacy with drug delivery and processes, they're affected by concepts and physics and chemistry and math.

Q. Please summarize for the Court some of your areas of research?

A. Yes. Most of my research has focused on applying material science to pharmacy problems. So I have done a lot of work with studying drug delivery and drug release, but I have also done a lot of work breaking down those things in component processes, for instance, I study drug excipient interactions, water interactions, water excipient interactions. I have also done a lot of modeling to explain those and develop and test to either corroborate the model or get data that we need.

Q. I'm going to pause here because I think I started too quickly and didn't give you a chance to get a glass of water.

A. I'm used to multitasking, so thank you. I'm good to go, thank you.

Q. Have you done any consulting work, Dr. Bellantone?

A. Yes, I have.

Q. And for whom have you done consulting work?

A. I have consulted for industry analyzing data and using that data to adjust dosage form and the design of dosage forms. I have also done work for the United States Food and Drug Administration and the work that I have done for the FDA, we have had a couple of projects with them developing new test methodologies and also exploring mechanisms by

which some formulations like nanoparticulate formulations work. And the ultimate goal there is to help the agency have a better understanding of generic and branded formulations.

Q. Can you please turn in your binder to DTX 106. Is DTX your CV?

A. Yes, that's my CV.

Q. Is the information contained in your CV accurate and up to date?

A. Yes, with the exception of maybe a couple of publications, a couple of graduate students and, of course, as I mentioned I retired from the University at the end of the fall.

MR. GAERTNER: Your Honor, we offer DTX 106 into evidence.

MR. CHEN: No objection, Your Honor.

BY MR. GAERTNER:

Q. Dr. Bellantone, have you previously acted as an expert in the area of pharmaceutical sciences?

A. Yes, I have.

Q. How many occasions?

A. Six or seven.

Q. Have you been accepted by a court as an expert?

A. Yes, I have.

Q. And by what court?

A. Actually it was here in Delaware, I testified before Judge Robinson on a pharmaceutical patent infringement case where I was a water excipient expert.

Q. What was the name of the law firm that retained you in that case?

A. Frommer, Lawrence & Haug.

MR. GAERTNER: Your Honor, at this time, we offer Dr. Bellantone as an expert in the field of pharmaceutical and material sciences, including surface and interface chemistry?

MR. CHEN: No objection.

THE COURT: All right. He's admitted as an expert. You may proceed.

BY MR. GAERTNER:

Q. Dr. Bellantone, what were you asked to do in this case?

A. I was asked to review Dr. Hoag's report and also review his test. And I was also asked to determine whether or not his test demonstrated that the so-called inner volume of granules of Zydus' ANDA product exhibited lipophilic properties.

Q. In your opinion, Dr. Bellantone, does the mesalamine blended compacted material produced by Dr. Hoag simulate the inner volume of the granules of the Zydus ANDA product?

A. No, it does not.

Q. If we could, let's first start with slide six if we could. Dr. Bellantone, did you have a chance to review the sources of the mesalamine and excipients that Zydus uses in its products and that Dr. Hoag used?

A. Yes, I did.

Q. Did Dr. Hoag use the same mesalamine and excipients that Zydus used in its product?

A. No. As you can see he used a supplier called Chemi -- I'm sorry, Zydus used Chemi and Dr. Hoag obtained them from AK.

Q. How about magnesium stearate, were there any differences there?

A. Again, different supplier, in the Zydus they used magnesium stearate from Lohmann and Dr. Hoag made it from Spectrum.

Q. With colloidal silicon dioxide, were there any differences there?

A. Well, it was the same supplier, but there was a difference. Evonik was the supplier for both, but Zydus' ANDA they used a pharmaceutical grade colloidal silicon dioxide and in Dr. Hoag's test it was a technical grade, technically would not be allowed in the pharmaceutical product.

Q. Can there be differences in the properties of the mesalamine and excipients made by different suppliers?

A. It's pretty well-known that even if you have the same

compendium grade say USP which refers to more chemical purity, there can be differences in physical properties, such as surface morphologies, the tablets, the particle sizes, shape, the surface energy of the particles and the ingredients.

Q. Can you have please turn to slide seven.

Dr. Bellantone, what do we see on slide seven?

A. This is something that I excerpted from one of the references in Dr. Hoag's report. It's a paper by Kayrak-Talay, et al., Quality by design for wet granulation in pharmaceutical processing. There is a little bit more to the title, but it was published in Powder Technology in 2013.

Q. What was stated in this publication?

A. Well, that publication noted that excipients are often derived from natural sources and a vendor can actually affect the properties and I'll read in that different outside vendors which can lead to variability in the excipient properties.

Q. And does this publication refer also to excipients derived from natural sources?

A. Yes, it does.

Q. And these excipients can lead to variability in excipient properties?

A. Yes.

Q. Now, is magnesium stearate an excipient derived from natural sources?
A. Yes, it is.
Q. In your opinion, Dr. Bellantone, should Dr. Hoag have assessed and controlled for any differences in the properties between the mesalamine and excipients that he used as opposed to the mesalamine and excipients that Zydus used in its ANDA product?
A. Yes, I believe so.
Q. Why is that?
A. Well, Dr. Hoag is attempting to make materials that he's going to test that will act as a surrogate because there was no tests done directly on the ANDA product, so you want to make sure that your surrogate reflects as accurately as possible the end product that you're using as a substitute for, knowing that there are variabilities in these, you would want to either control or make sure that there are no differences, and of course the easier way probably to do that is to get them from the same sources.
Q. Let's shift gears a little bit and talk about bulk density. Does the Zydus ANDA manufacturing process contain a bulk density specification that the roller compacted materials must meet to continue to be used in the Zydus manufacturing process?
A. It contains a bulk density specification, whether or

not it's roller compacted depends on whether it's failed that test.

Q. Before we get too far, can you explain to the Court what bulk density is about?

A. Yes, bulk density is -- it's a measurement or it's a test that you do, and it's a reflection of the properties of the granulars or whatever it is you're trying to assess, so it can reflect differences in surface energy, morphologies, core volume, porosities and so on.

Q. Do particle size and shape also affect it?

A. Yes, they do.

Q. If we could go to the next slide, please. Can you explain to the Court how bulk density is measured?

A. This is actually taken from the Zydus batch manufacturing record or BMR. This is section 6.2 and they give a very nice simple explanation of the protocol that's followed. You take a known weight of the powder or the granules that you want to test. You transfer that carefully into what's called a graduated cylinder which is the illustration to the right and you transfer the powder in. You're careful to level the powder without compressing or compacting.

And then what you do is you read the volume off of the cylinder and then you do a simple calculation where you take the weight of the powder that you put in divided by the

volume that you measured and that is your bulk density.

Q. You're referring to this section 6.2 in DTX 18?

A. Yes, I am.

MR. GAERTNER: Your Honor, at this time we move into evidence DTX 18.

MR. CHEN: No objection.

THE COURT: Admitted without objection.

BY MR. GAERTNER:

Q. Can we please go to the next slide. Dr. Bellantone, there is a lot of information on this slide so I would like to walk you through the portions of it. I would like to first start in the upper left-hand corner of this slide, and these also some sections from DTX 18 as well. If you could just read the section number, Dr. Bellantone. Let's start in the upper left-hand corner, what window do we see in the upper left-hand corner?

A. Well, in the upper left-hand corner this is -- these are the results that Zydus marked in its BMR and so what they -- what this shows is they took three samples out of their blended mix of magnesium stearate, colloidal silicon dioxide and mesalamine, they took three samples out of there, they determined the bulk density for all three then they took the average.

Q. And when you say the blended material, is this the blended material of mesalamine, colloidal silicon dioxide

and magnesium stearate?

A. Yes.

Q. This is this the blended material before it goes into the roller compaction process?

A. What they do is they test the bulk density right after the blending and if it meets the spec, then they don't have to roller compact, but if it fails the specification of .4 grams per ML, then they roll it.

Q. Did Dr. Hoag perform this test on material that he blended?

A. After the blending, Dr. Hoag determined the bulk density, yes.

Q. After the blending or after the roller?

A. After the blending and the roller compaction, he determined the bulk density, he recorded it and then he moved on.

Q. My question is before he roller compacted it when he did his blend, did he do this test?

A. No, not before.

Q. Moving to the bottom left-hand corner, Dr. Bellantone, what do we see there?

A. This is from the Zydus BMR again.

Q. You're referring to section 6.4?

A. Yes, I'm sorry, this is section 6.4 and 6.4.1. And this is after the failing the bulk density test, the

materials were roller compacted and then retested for the bulk density and this is the result of that determination. As you can see again they did three samples, took the average. And this time the average was .44 grams per ml, so it was above the criteria that they had set.

Q. Did the roller compacted material in batch EMM196 meet the Zydus bulk density specification?

A. Yes, it did.

Q. You touched on this a minute ago but I want to go back so we take it in order and that is Dr. Hoag's bulk density test. What do we see in the bottom right-hand corner of DDX 11.9?

A. There are two things shown here. Dr. Hoag blended a roller compacted pure mesalamine -- I'm sorry, he didn't blend, he roller compacted pure mesalamine. He also blended the colloidal silicon dioxide, the magnesium stearate and the mesalamine, he roller compacted that and you see the determinations of the two bulk densities.

Q. After he roller compacted the material, did Dr. Hoag test for the bulk density as specified in the Zydus manufacturing record?

A. No, he tested, he recorded it, but he didn't try to go back and meet the specification.

Q. When he tested it, did his material meet the Zydus bulk density specification?

A. No, it was below.
Q. Did Dr. Hoag go back then and roller compact the material again as the Zydus specification requires?
A. No.
Q. Did he record in his lab notebook why he didn't go back and roller compact it again?
A. No.
Q. Let's go to the next slide, please. In your opinion, Dr. Bellantone, is Dr. Hoag's failure to meet the Zydus bulk density specification render scientifically unreliable any comparison between the mesalamine blended roller compacted material that he created and the Zydus product?
A. Yes, I believe it does.
Q. Please explain to the Court your basis?
A. Well, a couple of things come out. First of all, by not meeting the spec, we have seen that the bulk density has an affect, so by not meeting the specification, he's going to go ahead and test something that actually never shows up in the Zydus ANDA product because had it failed they would have roller compacted before moving forward.

The other thing is, we were talking about some variabilities with excipients and process and so on. If you don't meet the bulk density, that's kind of a stopping point where you kind of check and look at what you have got. If you're not meeting it that should be a red flag that should

make you want to stop and go back and look why is it different because if I'm going to use this as a surrogate, I want to make sure that I'm as close as possible.

Q. Is there any indication in Dr. Hoag's lab notebook that he went back and examined his excipients and process at the time he failed to meet the bulk density specification?

A. No.

THE COURT: Mr. Gaertner, let me ask a question if I might. I understand your point that the substitute, you have a substitute that's as close as possible, explain to me as a matter of physical properties of these chemical compounds why it makes a difference, or should make a difference in testing, whether or not the Zydus ANDA spec of .4 is met? What's going on with the material that would make something denser, more or less of a lipophilic compound, if you understand what I'm asking.

THE WITNESS: Yes. If it's okay, I'll give a relatively concise answer here because this is going to be developed more fully as we go forward.

THE COURT: That's fine. If you got it worked into your routine, by all means, handle it on your own. But you talk about it now, so the answer that it's different doesn't really satisfy my question. So what if it's different? That's my question.

THE WITNESS: If I may just very quickly give

you a very concise answer so you can see where we're going. There are other properties besides lipophilicity that can affect the uptake of the water, for instance the core structure and things of that nature, they're going to be the reflection of differences in bulk density and so on. That's why we're calling attention to these things now, but they're going to be developed as part of my argument.

THE COURT: Okay. Go ahead, Mr. Gaertner, take it away.

BY MR. GAERTNER:

Q. Does bulk density have an impact on surface chemistry?

A. It's -- well, okay, it's a reflection of differences, it could be differences in the surface chemistry, it could be differences in the pore structure, the size of the particles, the shape of the particles and these as we'll see can affect the water uptake.

Q. Indeed that's where I was going, Your Honor. Does particle size, particle shape and pore shape, things of that nature impact the interaction of materials in water?

A. Yes, it interacts, it can interact with the interaction, it can also affects the kinetics and the rates of uptake.

Q. I would like to go to the next slide, 11.11, please. Now, Dr. Bellantone, we just discussed Dr. Hoag's failure to meet the bulk density specification. On 11.11, can you just

illustrate for the Court what point in the Zydus manufacturing process the bulk density test comes in?

A. It's in the -- Zydus actually in their BMR breaks things into a couple of -- they give names to processes, so they have got their compaction group and the bulk density determination occurs in that compaction step. It has to be met before it moves on to further steps.

Q. Now, did Dr. Hoag in making his tablets that he tested deviate from the Zydus ANDA process in any other way?

A. Yes, I think if we move forward, what he did was he roller compacted, noted the bulk density, but then he deviated from the process by introducing a compression step. He actually took the -- what came out of the roller compactor, then he compressed it into tablets.

Q. Now, did this step exist in the Zydus manufacturing process?

A. No.

Q. Now, did doctor Hoag report in his lab notebook the settings that he used to compress these tablets?

A. No.

Q. What is the next step in the Zydus process once the roller compacted material meets the bulk density specification?

THE COURT: Hold on just a moment.

Does compression have the same or similar effect

as compaction?

THE WITNESS: It depends on the, the settings, because when you come out of the compactor, you have the granules and you sift them to get the size. And if you compress them into a tablet, among other things, what you are doing is you're squeezing out a lot of the waste basis, and as we'll see, that's kind of an important thing.

And the compression step in making the tablet can also introduce some variability and reproducibility into the process that he's following.

THE COURT: As a generalized matter, though, do compaction and compression increase bulk density?

THE WITNESS: You would -- oh, yes. Well, certainly, the compression. Compaction, you would expect would increase the bulk density because you're squeezing the particle closer together, so you are squeezing out some of the empty space and when you compress it into a tablet, again, you're squeezing out more of the empty space. So that would increase the bulk density.

THE COURT: All right. Thank you. Thank you, Mr. Gaertner.

BY MR. GAERTNER:

Q. Can the force of compression settings also impact the up take of the water into a tablet?

A. Yes.

Q. And did Dr. Hoag report in his lab notebook whether the compression settings he used to make his tablet at this phase in any way align with the compression settings that Zydus used when it ultimately makes its ANDA product?

A. No.

Q. Let's move along. The last question I believe I had was, what happens next after, in the Zydus process, the roller compacted material comes out, meets the bulk density specification. What happens next?

A. Okay. After you go through the compaction and meet the specification, then you move on to what's called the wet granulation, which is actually a combination of you're blending a couple of hydrophilic polymers and then you're adding water to wet, that's why they call it wet granulation. So there's a significant amount of water that's added into that step. At the end of all of that mixing, then you dry the materials.

Q. All right. And what's the next step then, Dr. Bellantone?

A. After that, then you move onto what they call the lubrication step. So they blend in some more colloidal silicon dioxide, some microcrystalline cellulose, which is another polymer, and then they blend in some magnesium stearate. And then after they've done all of that, then they, if you click one more time, then they do the tablet

compression.

Q. Now, I want to --

THE COURT: I'm sorry, Mr. Gaertner. I do this quite a lot.

MR. GAERTNER: No. Please do.

THE COURT: So I've heard a lot of people talking about lubrication. What does it mean to you to say lubrication in the context of a series of steps like that? What's being lubricated and for what purpose?

THE WITNESS: Okay. When you are compressing into tablets, you're actually putting thousands of pounds per square inch to get the materials to stick together into a nicely formed coherent tablet.

One of the problems that you can run into is that after you put the pressure on and you release it, the materials can stick to the, to the walls of the -- so you've got to punch and die. If it sticks to the walls when it gets ejected, you can break the tablets, or you can introduce like cracks, things like that.

So you put a lubricant so it flows out more smoothly and you avoid all those types of imperfections associated with ejecting it.

THE COURT: Thank you.

Mr. Gaertner?

BY MR. GAERTNER:

Q. I want to focus here on the wet granulation step that we talked about.

Do the subsequent processing steps in the Zydus ANDA process, in particular, wet granulation step that Dr. Hoag did not perform affect the properties of the compacted materials and the Zydus ANDA product?

A. Yes. Yes, they do.

MR. GAERTNER: Can we go to the next slide, please.

Next, please.

THE WITNESS: Okay. It's pretty well-known in the literature, and it has been reported that wet granulation does have effects and what it -- what I have here, I compared a -- an excerpt from another one of Dr. Hoag's references. This paper is by Hapgood, et al, and it's called the "Drop Penetration into Porous Powder Beds." It was published in the "Journal of Colloidal and Interface Science" in 2002.

And they talk in that paper, among other things, that wet granulation is complex. Many phenomenon occur simultaneously with the granule attributes and then they list some things. But among the attributes that can be modified are the granule attrition, which is kind of the wearing down and breakage. So you can actually break up the granules was part of that step.

Q. Dr. Bellantone, for purposes of the record, could you read in the slide that you just discussed?
A. Yes. This was DDX-11.16.
Q. And the reference, please?
A. Yes. It was Hapgood, et al, Drop penetration into porous powder beds, published in 2002 in the "Journal of, Colloidal and Interface Science."
Q. And the highlighted material?
A. Yes. The wet granulation is complex. Many phenomena occur simultaneously in the granulator which will influence the granule attributes. We divide these into three groups: Granule nucleation and binder distribution. Granule consolidation and growth. And granule attrition and breakage.
Q. Now, Dr. Bellantone, in your opinion as an expert surface and interfacial chemistry, does Dr. Hoag's failure to control for the differences in the mesalamine and excipients he used and his failure to follow the Zydus ANDA product render scientifically unreliable any comparison between the mesalamine blend roller compacted material that Dr. Hoag created and the Zydus ANDA product?
A. Yes. I think there are too many unknowns, too many steps that are significant that would affect the surface properties and the shapes in the particles and the porosity and things of that nature that we'll talk more about. I

just think that there's too much of a difference to draw any comparison.

Q. Now, did Dr. Hoag run his capillary method on the granules that he created?

A. No. Not on the granules. He, what he did was he actually ran his test on tablets that he compressed out of the granules.

MR. GAERTNER: Could we please put up Dr. Hoag's lab notebook, please, which I believe is DTX-117. Is that right? We have a PTX-version up here. PTX-577.

BY MR. GAERTNER:

Q. That's up on your screen as well, I think, Dr. Bellantone.

A. Mm-hmm.

Q. And this is a copy of Dr. Hoag's lab notebook.

And could you read for the Court what the purpose of Dr., I'm sorry, the purpose recorded for the experiment that Dr. Hoag created?

A. Yes. Well, it says the purpose, to make mesalamine tablets by roller-compaction technique.

Q. And if you could turn to page 5 of Dr. Hoag's lab notebook, it's in your binder as well as on the screen. We can take it up.

And a page 5 at the top of the lab notebook, did Dr. Hoag record the tableting procedure?

A. He recorded most of it. He recorded the weights. He recorded that he put it into a Stokes press, but he did not record the compression force.

Q. And for the benefit of the Court, what's a Stokes press?

A. It's an apparatus used to make tablets.

Q. And further down on the page of Hoag lab notebook page 5, PTX-577, can you read for the Court the headings that he had where he recorded the data on his test?

A. Yes. Well, it starts with tablet number and then he has got the tablet weight, the tablet height, the tablet diameter in centimeters, the tablet volume, and then the percent porosity.

Q. Now, on this page on 5 of Hoag's lab note, did Dr. Hoag also describe his capillary experiment?

A. Yes. That's where he describes it.

Q. And can you describe what he did for the Court?

A. Yes. He filled a capillary tube with water up to a marked point and then a tablet was placed underneath the capillary tube on a rising platform. Then he, he raised it until the capillary made contact with the tablet surface. Then they recorded the time for the water to absorb into the tablet.

Q. Okay. And did Dr. Hoag record the volume of the water that he put in the capillary?

A. No, he did not.
Q. Did you estimate the volume of water that's in the capillary?
A. Yes. From his report and the photographs in his report. And knowing that the tablet size was 13 millimeters, I was able to reference everything in the photographs in his report, so I was able to actually calculate the height of the capillary. I was able to estimate the diameter and it corresponded very much with the standard off-the-shelf capillary that you can buy for use in the lab.

So from that procedure and knowing the height of where the mark was that he put, I was able to calculate pretty, pretty closely what volume of water he was introducing.
Q. And what did you estimate that volume of water to be?
A. I estimated it to be 57 microliters.
Q. Now, in the Hapgood reference, which Dr. Hoag normally didn't follow, but that's a drop penetration test. Does that reference describe the volume of the droplets that was used in the drop penetration test in Hapgood?
A. Yes.
Q. And what was the range of the water droplets there?
A. Yes. There was a range, but it was from about maybe six to eleven microliters.

THE COURT: Give that to me again. What was the volume that you calculated Dr. Hoag had used in his test?

THE WITNESS: It was 57 microliters.

THE COURT: And what did you say was the drop penetration volume in Hapgood's test?

THE WITNESS: It varied, but it was six to eleven.

THE COURT: And what difference does it make whether you use 57 milliliters or six or seven milliliters?

THE WITNESS: Okay. You're very good at anticipating, but the actual volume, later on, I'm going to compare that to the volume of the space in the tablet and make the argument that it's large.

THE COURT: I'm sorry. I'm ahead of you.

THE WITNESS: That's fine.

MR. GAERTNER: You're reading ahead, Your Honor. You're reading ahead.

THE COURT: You just go ahead, Mr. Gaertner.

MR. GAERTNER: I will try my best. I will try my best.

BY MR. GAERTNER:

Q. Dr. Bellantone, did Dr. Hoag in performing his test control for all the variables that you believe a reasonable scientist would control for in performing a test such as he

described?

A. No, I don't believe so.

MR. GAERTNER: Can we go to slide 11.19. Oh, let's go to the next one. Okay.

BY MR. GAERTNER:

Q. First of all, Dr. Bellantone, did you notice any -- you talked a few minutes ago -- I will start fresh. Withdraw everything I said.

You talked a few minutes ago with the Court about the impact of lubricants and things like that in tablet ejection.

Did you notice any imperfections in the tablets that Dr. Hoag made that were pure mesalamine without any lubricant involved?

A. Yes. Actually, as you can see in the photograph, there are some imperfections. From this angle you can really see them sort of along the bottom. There are no, no pictures taken specifically of the top, but, you know, it raises the question of imperfections all over the surface.

Q. You are referring to now the screen shot at time 3:02 at PTX-581?

A. Yes. Yes.

Q. Now, how can surface imperfections affect the rate of water absorption into a tablet?

A. Well, it can do it actually in a couple of different ways.

First of all, when you make the contact between the capillary tube and the surface, it will make a difference if you're making a contact in a smooth area, or if you are, if there are -- you know, either roughness or voids or cracks.

The other thing that it raises the question of is whether there are also, in addition to on the surface, if there are internal imperfections, and as we'll see later on, if there are, that could affect the rate of the water up take as well.

Q. Let's go to the next slide. And I may have -- I'm sorry. Let's go back. I may have missed this when I was talking to one of my colleagues here. I will move along. We will go to the next slide.

Dr. Bellantone, were you in the courtroom when Dr. Hoag testified?

A. Yes.

Q. And you heard him testify that he made sure that his capillary tube was vertical and that it was perpendicular to the surface of the tablet?

A. Yes.

Q. And you also heard him testify that once the capillary tube was mounted, it was not moved or altered?

A. Yes.
Q. Now, in reviewing the photographs and movies of Dr. Hoag's test, did you observe any indications that the capillary tube that Dr. Hoag used was not perpendicular to the surface and, in fact, moved during the course of his test?
A. Yes. Actually, this, this picture, DDX-11.21 actually shows that. This is a side-to-side deviation from a right angle, so the tube is not perpendicular with the tablet surface. And that side-to-side, if you keep in mind this is a two dimensional photograph even front to back is possible, but it wouldn't show up in the picture.
Q. And would this irregular movement and placement of the capillary affect the recording of the time for any water absorption?
A. Potentially, it very could, yes.
Q. Did Dr. Hoag adequately control for pore radius and length and pore size, shape and orientation in his test between his mesalamine only tablets and his mesalamine blended tablets?
A. No.
Q. Have you prepared any demonstratives to help illustrate your opinion?
A. Yes.
Q. Can we go to the next slide? We're looking now at

DDX-11.22. And could you please explain to the Court what we see here?

A. Yes. This is actually getting to what we were anticipating a short while ago.

First, what I'd like to do, explain what porosity means. If you have a tablet, the total volume of the tablet, including the material and the empty space would be, would be -- that's the total volume. The porosity would be the fraction of that total volume, that is the empty space, so that would be the pores.

And so basically you take the total volume of the pores, compare that to the total volume of the tablet, and that's your porosity.

The reason controlling for porosity is not sufficient to know about the pore structure and the pore size is because there are any number of ways that I can have pores that add up to the same volume. And so I could have more small pores or fewer large pores already, say, in terms of the pore diameter or radius. They could add up to the same total volume, so they would have the same porosity, but I would have very different pores.

If we go to the next, I kind of amplify that. So on DDX-11.23. Another consideration is the pore shape and the orientation or geometry.

The on left you can see you can have, say, many

smaller pores that could be jagged, not straight. They could branch. They could have dead ends, things of that nature, or I could have fewer pores that are, say, relatively larger, and taken all together, that is going to have a very profound impact on the rate of the water uptake.

Q. And when you refer here to pore size, radius and the various terms that you used, you are now talking about the pores that were in the, the tablets that Dr. Hoag made; is that correct?

A. In this context, yes. I'm referring to what's in the tablets.

Q. And did Dr. Hoag measure or control for pore radius, pore length, pore shape and orientation?

A. No, he did not.

Q. Now, can the differences in pore radius, in pore shape and pore orientation affect the rate of water uptake between the two tablets, two types of tablets, I should say, that Dr. Hoag created?

A. Yes.

Q. Can we go to the next slide, please.

A. It's, it's recognized in the literature, and it's also common -- sort of intuitive that if you are trying to pull something in and you are trying to force it through small curves or branch, it's going to be harder, so it would be

slower.

So I've excerpted again from the literature, and this again is the Hapgood paper, drop penetration into porous powder beds published in the "Journal of Colloid and Interface Science" in 2002.

And three -- and three places in that paper, they discuss this point.

First, I will read it. Imbibition of a single drop into a porous substrate depends on the structure of the substrate: The porosity, the size of the pores, the orientation of the pores, and the surface chemistry.

THE COURT: What is imbibition?

THE WITNESS: Oh, yes. Imbibing is where a liquid will be drawn into capillaries or pores, and we call that imbibing or imbibition.

THE COURT: Thank you.

THE WITNESS: Later on in the paper, the paper says, changing the powder properties will alter the size distribution of pores in the powder bed. This may assist or restrict motion into the bed.

And then elsewhere in the paper later on it says, the effect of porosity on penetration time cannot be evaluated without considering pore size.

Q. Now, this paper deals with powder beds; is that correct? All right. But the same considerations apply when

you compress powder into a tablet as well; is that correct?

A. Yes. From a scientific standpoint, you have a packed powder or a compressed powder. The concepts are the same, so there's no difference in the applicability.

Q. Dr. Bellantone, in light of your, in light of the imperfections that we've seen in the tablets, the inconsistent positioning of the capillary and the failure to check for pore radios, length shape and orientation, can one reach a scientifically reliable conclusion that the difference in water absorption time that Dr. Hoag observed is between his mesalamine only tablets and his mesalamine blended tablets is due to the presence of magnesium stearate in the mesalamine blended tablets?

A. Well, you cannot reach any valid conclusion that the magnesium stearate is causing any resistance to the water uptake, so the magnesium stearate is not imparting any kind of a lipophilic nature. You can't make that conclusion at all.

Q. Did Dr. Hoag isolate the variables that will be necessary to make that conclusion?

A. No, he did not.

Q. Now, Dr. Bellantone, you've listed many criticisms of Dr. Hoag's methodology and application of his test, but if you suspend those for the moment and put those to the side

and actually credit Dr. Hoag's tests, do those tests, in your opinion, establish that the so-called inner volume of the granules of the Zydus ANDA product exhibit lipophilic property?

A. No, they don't. And I want to be clear that, you know I don't credit, but even if you did, it's not sufficient and does not establish the, any lipophilic nature.

Q. And did you provide a demonstrative to help explain your opinion to the Court?

A. Yes. If we go to the next. There are actually three components to this argument, and I think this will get to an earlier question as well.

First, the mesalamine blend compacts that Dr. Hoag prepared, as did the pure mesalamine, they both started to take up water as soon as it was introduced. This picture compared to what happens at eight seconds, and they both started to take the water up immediately, and there was a significant amount taken up by eight seconds.

Further, all of the water that was introduced was taken up by both the pure mesalamine and the blended mesalamine. So it starts taking it up immediately and it takes up all the water that was presented. And if you had looked at the movies and the photographs, you would have every reason to expect that if more water had been introduced, more water would have been taken up.

Q. Now, during the first eight seconds of Dr. Hoag's test, did both types of his tablets absorb water at the same rate?

A. Comparable rates.

THE COURT: What does that mean?

THE WITNESS: Well, as you can see, they're almost, they're almost the same. So to me, when I say comparable rates, you know, I didn't measure exactly, because Dr. Hoag had measured the actual time for a complete absorption, because you can see the amount of the drop between, below the line was, they were consistent, without getting into quantitative.

THE COURT: All right.

BY MR. GAERTNER:

Q. Now, you were in the courtroom yesterday, or the other day rather when Dr. Hoag testified that his conclusion was based on the statistical difference between the water absorption time between his mesalamine only and mesalamine blend tablets?

A. Yes.

Q. All right. In your opinion, did the statistical difference between the water absorption time between the two samples mean that one sample is lipophilic?

THE COURT: Hold on.

MR. CHEN: Your Honor, I've been trying not to

be disruptive, but there are several leading questions. I object to that question.

MR. GAERTNER: I asked, in your opinion.

THE COURT: Give me the question back.

(The court reporter read back the question as follows.)

"Question: Right. In your opinion, did the statistical difference between the water absorption time between the two samples mean that one sample is lipophilic?"

THE COURT: Overruled. You can answer.

THE WITNESS: Thank you. No, I don't think that I am suggesting that at all.

BY MR. GAERTNER:

Q. Now, are there any reasons why it is your opinion that Dr. Hoag's test actually established the tablets created from Dr. Hoag's mesalamine blend tablets do not exhibit lipophilic characteristics?

A. Yes. Well, actually, if we could go back. Thank you.

The second thing is that it was, as it turns out, a large amount of water. It was taken up in what I consider to be a very short period of time for the blended mesalamine while the water was taken up at roughly 111 to 139 seconds.

To my way of thinking, that is very rapid. If

you compare these results with say drop penetration tests for admittedly more lipophilic compounds, those drops which are smaller than this can actually take up to a couple of hours to be taken up. So, you know, one or two minutes on an absolute scale is very, very rapid.

Q. Okay. I am sorry. Did you finish your answer?

A. Yes.

Q. I'm sorry if I got ahead of you. Let's go onto the next slide, please.

A. Okay.

Q. We're on slide DDX-11.27. Can you explain to the Court what we see here?

A. Yes. It's another way, an objective and valid way to assess whether or not the substrate likes water. And in this, I'm actually looking at the total amount of water that is being take taken up.

As we discussed earlier from Dr. Hoag's notebook and his photographs and his data, and from nothing else, that's all I needed, I was able to calculate, excuse me, the total void space in his tablets. I was also able to calculate the total amount of water that was being introduced, so I did a comparison. And it turns out that the water that was introduced actually filled up about 35 percent of the void space and it did it very rapidly.

And so I think I have a movie here. I hope it

works. Okay. It probably doesn't. That's okay. Oh, there we go.

What this is indicating is that, is that the water is being introduced, it's penetrating down and spreading out. And one of the calculations that I did to sort of interpret the magnitude of that was I compared the contact area between the capillary and the tablet to the total surface area of that face of the tablet and it turns out that the contact area was .71 percent, which is about one over 140.

So the contact area was one one-hundred-and-fortieth, but in about two minutes it filled up about a third of the total pore space, so it had to spread out in the tablet very significantly. And as I said, there was every reason, and every indication to think that if more water had been introduced, that process would have gone to an even higher fraction.

So --

THE COURT: And would you tell me again how you figured that 35.2 percent of the void space was filled?

THE WITNESS: Yes. Dr. Hoag recorded the dimensions in the volume of his tablet. He also had determined the porosity of his tablet. That was in his notebook.

So by multiplying that fraction times the total, I was able to get the volume of the voids. By measuring the height and diameter of the capillary, I was able to estimate the volume of the water that was being introduced.

THE COURT: Okay. Thank you.

BY MR. GAERTNER:

Q. In your answer to Judge Jordan, Dr. Bellantone, you made a statement. I want to make sure the record is correct.

You noted that Dr. Hoag calculated porosity. I want to make sure. Is that the same thing as pore size, pore shape, pore orientation, pore radius and the things that you talked about before?

A. No. Actually, that's one of the, one of the things that is very important about this. The porosity is not the same as the pore size, shape, or other characteristics. This analysis only uses the porosity. It does not need any, any information about the, the size or the character of the pores.

This is just looking and saying that I've got a substrate and it soaks up a very large amount of water in a short amount of time, so from that standpoint. And the extent of the uptake is another objective measure of whether or not something is lipophilic or hydrophilic.

Q. And in conclusion, Dr. Bellantone, in your opinion,

does Dr. Hoag's test establish the compacts that he created in his mesalamine blend tablets exhibit lipophilic characteristics?

A. No. They do not. In my opinion, given, you know, especially the, just to finish up on the extent, that indicates that is not lipophilic. That really indicates that it's hydrophilic, very significantly so.

So his compacts are not indicating any kind of lipophilic behavior and so just the mere presence of having say magnesium stearate, he does not prove that just that mere presence affects the, the affinity for water.

MR. GAERTNER: Your Honor, at this time I'd like to move into evidence PTX-577. It might be in, but I just want to make sure it's in. And then the still shots that we have in the demonstrative, which are Hoag video time 3:03, PTX-581; Hoag video at 3:02, PTX-580.

THE COURT: Mr. Chen.

MR. GAERTNER: Your Honor --

THE COURT: I think your opposing colleague would like to talk to you.

MR. GAERTNER: I have 577 as the lab notebook.

MR. CHEN: No objection.

THE COURT: Okay.

(Exhibits admitted into evidence.)

MR. GAERTNER: And, Your Honor, just to make it

clear, we will then stamp the DTX numbers on those images and we'll put them in.

THE COURT: All right. They're admitted without objection.

Now, let me -- now, I'm conscious that you all are trying to keep your experts and your other Zydus' experts within the bounds of what their report said and everything, so sometimes as I'm asking questions, I hope I'm not moving people outside where they ought to be.

Rather than just ask this question of Dr. Bellantone straight up, I will ask more generally. In the course of his testimony, we looked at a series of slides which broke down the Zydus manufacturing process by steps. There was some discussion of the wet granulation phase. Right? I'm wondering whether the wet granulation phase has any effect on chemical properties as opposed to just physical properties, if you understand what I'm asking. And I don't know whether that is in anybody's expert report or anybody has opined on that.

I'm not asking for attorney argument on it right now, but just -- and if you've already, you know, if it has come out in the course of somebody's discussion already and I wasn't sufficiently attuned to the testimony to pick it up, my apologies. You could maybe point that out to me in one of the dailies that you already got. But that's a

question that has come up in my mind.

MR. GAERTNER: I mean, to be fair to everybody, Dr. Bellantone is an expert on the interfacial and surface chemistry, so he talked about the impact on the surface properties.

THE COURT: Right.

MR. GAERTNER: And how it would absorb water.

THE COURT: Right.

MR. GAERTNER: So I --

THE COURT: So that's why I'm not asking him.

MR. GAERTNER: Yes.

THE COURT: But I am wondering if anybody is going to talk about that. Maybe not. And then that will just be a question that stays out there, which is okay. Some questions remain unanswered in this life.

All right. Did you have any other questions for Dr. Bellantone?

MR. GAERTNER: No, Your Honor.

THE COURT: All right. Cross-examination.

MR. CHEN: Thank you, Your Honor.

May we approach, Your Honor?

THE COURT: Yes, you certainly may.

(Mr. Chen handed notebooks to the Court and to the witness.)

MR. CHEN: May I approach the witness?

THE COURT: Yes.

CROSS-EXAMINATION

BY MR. CHEN:

Q. Dr. Bellantone, we have not had a chance to meet. My name is Angus Chen. I'm counsel for plaintiffs. Apparently, I live in a town just north of you in Hastings on the Hudson.

A. Oh.

Q. Nice to meet you.

A. You are my neighbor.

Q. Yes.

A. Good morning.

Q. Good morning.

I'll just start with a couple of background questions. None of the controlled release formulations, oral pharmaceutical formulations that you work on contain mesalamine; correct?

A. That's correct.

Q. And none of the controlled release oral pharmaceutical formulations that you worked on contain an inner lipophilic matrix; correct?

A. As defined here, you know, in other context perhaps, but as defined here, that's correct.

Q. And you have not been elected to the USP counsel of experts; correct?

A. That's correct.

MR. CHEN: Can we put up Dr. Bellantone's demonstratives, please. Let's start with -- let's go to his last slide at the conclusion, DDX 11.28.

BY MR. CHEN:

Q. This is the demonstrative that you just put up at the end; right?

A. Yes, I recognize that.

Q. I'm curious, I didn't hear any opinions about the third bullet. Dr. Hoag's test has never been published in a peer-reviewed journal is not the recognized drop penetration test and is scientifically unreliable. Do you see that?

A. Yes.

Q. Do you stand by that statement?

A. I was not asked about that, but I would be happy to discuss it.

Q. Do you stand by it?

A. Yes.

Q. I received these slides last night, so I just want to check because I didn't hear about it. Okay?

So can we put up the picture of, from Dr. Bellantone's slides of Dr. Hoag's test. Let's go to DDX 11.26, please.

That's an image of Professor Hoag's test; right?

A. Yes.

Q. Now, what Professor Hoag did in his method of

conducting the drop penetration test, he recorded the time for water to drain from a filled capillary placed into contact with the compressed powder surface; right?

A. Yeah, he recorded the total time for it all to drain, yes, that's right.

Q. And so your opinion is that a capillary method for conducting the drop penetration test has never been published in a peer-reviewed journal; right?

A. I have never seen it published in a peer-reviewed journal, that's correct, I believe Dr. Hoag admitted the same thing.

Q. You were in the room when he testified; right?

A. Yes.

Q. That's your recollection, that was his admission?

A. Not there, perhaps I was informed by counsel about his deposition.

MR. GAERTNER: We are going beyond the scope, Your Honor. Mr. Chen first chastised the scope of Dr. Hoag's direct testimony, now he's --

THE COURT: I disagree. It's fair cross-examination, Mr. Gaertner.

BY MR. CHEN:

Q. Can we go to the last slide. A minute ago I heard you say that you have never seen the capillary method for drop penetration published in a peer-reviewed journal; right?

A. That's correct.
Q. Your slide says that test has never been published in a peer-reviewed journal. So is it just that you have never seen it or it's never been published?
A. That's a semantic issue. I will say that I have never seen it, and you know, I will stand by that statement, yes.
Q. Okay. So it's different statement, then; right?
A. I'll give you that.
Q. You have a binder in front of you. Can I ask you to turn to tab D, please. Do you see that it's an article from the Journal of Pharmacy and Pharmacology 1979?
A. What tab is that, please?
Q. It's called Bellantone D.
A. Yes.
Q. And if you turn after the first page, and I'm looking at the first page of the actual publication, it's a communication in the Journal of Pharmacy and Pharmacology 1979. By the way, do you know if it is that's a peer-reviewed journal?
A. Yes, it is.
Q. It's entitled, Apparent validity of the Washburn equation when applied to compressed tablets by an M.J. Groves and M.H. Alkan from Chelsea College, University of London. Do you see that?
A. Yes.

Q. On the left-hand column, it says Groves and Alkan say the micro method used consist of recording the time for the liquid under examination to drain from a filled two microliter capillary when placed into contact with the tablet surface. Did I read that correctly?

A. Yes.

Q. And a moment ago we agreed, right, that's what Professor Hoag did, he recorded the time for water to drain from a filled capillary when placed into contact with a surface?

A. I'm not seeing a picture here, but I will, you know if it was the same vertical setup and so on, yes.

Q. Now, let's turn to tab Bellantone F in your binder, please. Let me know when you're there.

A. Okay. I'm here.

Q. Do you see this is a thesis?

A. Yes.

Q. Entitled a study of some physical properties of compressed tablets containing drugs, a thesis by an M.H. Alkan from the University of London Chelsea College. Do you see that?

A. I see that.

Q. If I could ask you to turn to page 112 of the thesis. The page numbers are at the top of the page.

A. Okay. I'm there.

Q. Do you see there is a heading, 4.1.3, liquid penetration measurement techniques?

A. Yes.

Q. The sentence above that says that Ganderton 1969 showed that magnesium stearate prevented the penetration of water into tablets by virtue of its high contact angle with water. Did I read that correctly?

A. Yes.

Q. We have heard a lot of discussion about magnesium stearate, sometimes it's used as a lubricant in the pharmaceutical industry; right?

A. Right.

Q. Let's turn back a few pages, page 22, the same document.

A. Which page?

Q. 22, please. Let me know when you're there, please.

A. Okay.

Q. All the way at the bottom of the page, the very last paragraph, Alkan, Dr. Alkan states lubricants are generally hydrophobic substances and they cause an increase in the disintegration time by preventing water wetting and penetration into the tablets. It carries over into page 23. Did I read that correctly?

A. Yes.

Q. A moment ago you asked for a picture to verify Dr.

Grove's and Alkan's setup, do you recall that?

A. I do.

Q. Let me turn to page 118 now. Please let me know when you're there.

A. Okay.

Q. At the top of the page there is a section entitled 4.2.2.4, measurement of the penetration rate. Do you see that?

A. Yes.

Q. And in the second paragraph under the method, Dr. Alkan says that the pipet was filed with the liquid under investigation and placed in vertical contact with the upper flat face of the tablet resting on a horizontal surface (Figure 4.3). Do you see that?

A. Yes.

Q. On page 119, the next page is a Figure 4.3; right?

A. Yes.

Q. Do you see a vertical capillary there?

A. Yes, I do.

Q. And that resembles what Professor Hoag did; right?

A. Yes.

Q. Now, turn to page 120, please, sir. Are you there?

A. Yes.

Q. In the first paragraph, third sentence in, Dr. Alkan states the tablet pore structure may also be assumed to be

reasonably homogenous. Did I read that correctly?
A. Yes.
Q. I think earlier you testified whether it's a powder bed for a compact or a tablet, the same principles apply; right?
A. Yes, unless it's a very loose powder bed, that's correct.
Q. Now, turn to page 144, please. Are you there?
A. 144, yes.
Q. And there is a discussion, 4.4, and the first paragraph under there in the third sentence, Dr. Alkan explains further, since the average penetration length was calculated from the volume of the penetrated liquid, the tortuosity and the pore shape factors necessary for viscous flow did not require to be considered. Did I read that correct?
A. Yes. That sentence, yes, you read that correctly.
Q. I'm sorry, with all due respect, my question was did I read that correctly?
A. Yes, you did.
THE COURT: Is there going to be something where we get from something where we get from reading this to a question? I mean, you have been asking him to read things, you have been reading them correctly, he may be wondering, I'm certainly wondering where are we going?

MR. CHEN: It's simply I believe I asked him a minute ago to confirm that he testified earlier that powder beds and tablets, the same principles apply.

Q. My question is, so isn't it possible that the same principles apply here with respect to Professor Hoag's test that pore size and the pore shape factors do not need to be considered?

A. No, I disagree with that.

Q. It's not possible?

A. I disagree with that.

Q. I just want to briefly turn back to Bellantone D, please, the Groves article. Do you recognize that article?

A. That was D. No, I have never seen that article until now.

Q. Are you sure about that?

A. If I have seen it, I don't recall it.

Q. That's fair. But you're fairly certain that you have never seen it before?

A. Well, you seem to be fairly certain that I have, and I don't recall seeing it, so I'll just say I don't recall seeing it before.

Q. Actually I wasn't certain one way or the other, I was just asking.

Can you turn to tab G, please. Do you recognize this document?

A. Yes, I do.
Q. It's a Ph.D. thesis by an Amar Venkatarangan?
A. Venkatarangan.
Q. V-e-n-k-a-t-a-r-a-n-g-a-n; right?
A. Yes.
Q. And you were on the advisory committee for Amar V's thesis; correct?
A. Yes.
Q. And that's your name on the front page; right?
A. Yes, it is.
Q. And that's your signature approving his thesis?
A. Yes, it is.
Q. And was Mr. Venkatarangan awarded his Ph.D.?
A. Yes, he was.
Q. Did you know that after he graduated he went on to become a scientist at GlaxoSmithKline?
A. Yes.
Q. Turn to page 21, please, of Dr. Venkatarangan's thesis.
A. Where is that?
Q. It's the page numbers on the bottom.
A. I'm sorry, which tab, please?
Q. We were in Bellantone G; right?
A. Page 21, you said?
Q. Yes, sir.

A. Okay.
Q. Are you there?
A. Yes.
Q. You see the section 3.6, fluid dynamics and capillarity in other fields?
A. Yes.
Q. Dr. Venkatarangan says that the liquid and fluid flow dynamics were widely studied by scientists in the field of capillary and soil sciences. And he cites to reference 113, among others; right?
A. Yes.
Q. I gather from your reaction you know where I'm going. Turn to page 181, please.
A. 181, you said?
Q. Yes. Reference 113, it's the Groves and Alkan article we were just discussing; am I correct?
A. Yes.
Q. Do you routinely form opinions without considering all the relevant background information?
A. Well, I think that's -- I think that's a bit of a misphrased question. First of all, I was on his advisory committee, I was not his major advisor. And the role of me as an associate advisor is he comes to me with questions, you know, we discuss various aspects, it is not for me as an associate advisor to necessarily filter through every

reference. It is for me to sort of act as an advisor and partially as a screener to make sure that the science appears to be okay. In that capacity, I did not read every reference. I don't have time to read every reference for everything. I think that's a standard practice.

So if you want to ask if I have seen that reference, no. If you want to ask if I had any opinion that I expressed in his dissertation, again, the answer is no. If you want to ask if I consulted, if he consulted with me and so on with questions, yes, absolutely. But my role was not the screen or check all of his references, for instance.

Q. You approved his thesis without checking all of the references?

A. Oh, sure. Yeah. I thought the science was fine.

Q. Let's talk about some of the criticisms that you had of Professor Hoag's test.

Can we go to Dr. Hoag's demonstrative PDX 5.1. You were in the courtroom when Professor Hoag testified. Do you remember this demonstrative?

A. Yes.

Q. Now, you agree that you have no reason to doubt that his control compact had a hundred percent mesalamine; right?

A. Yes, that's correct.

Q. And you have no reason to doubt that his test compact had 99.3 percent mesalamine; right?

A. Yes.
Q. And his test compact only had .33 percent magnesium stearate; right?
A. To be honest, I didn't bring this point up, but it was in my report. We're not sure exactly how much because when you followed his procedure, in his notebook, he mixed the magnesium stearate with the colloidal silicon dioxide before sifting, so by virtue of the mixing, you don't know when he transferred the weight, you don't know if it was the same fraction. So if it sounds like I'm hemming and hawing, they were I believe known to interact, so I'll give it to you, but reluctantly.
Q. Roughly .3 percent magnesium stearate, you agree?
A. Yes.
Q. That's a really small amount of magnesium stearate, isn't it?
A. Yes.
Q. And that's such a small amount of magnesium stearate, that really shouldn't have an affect on the compound, should it?
A. Well, it depends on the properties that you're talking about. So I'm not sure exactly where you're going, but let me just say that in terms of affecting the bulk performance, say the bulk solubility of the magnesium stearate, how much will dissolve in water and so on if I just let it sit there,

no, you would expect it very small.

However, in terms if it's acting as a lubricant or something like that, then in terms of his tests, the imperfections that might be avoided by a lubricant could be very profound when you compared a little lubrication to no lubrication.

So I'm not trying to sort of do a dance, but it depends on what you're looking at, because I think that in terms of certain bulk properties, that amount is not going to have an affect, but in other say collective properties that are indirectly tested, so water uptake, yes, it could.

Q. So there are some properties where a very small amount of magnesium stearate could have a significant impact?

A. Yes, if you take those caveats into consideration, I'll give you that.

Q. One of them you said was a lubricant property?

A. Yes.

Q. And a moment ago we saw in Dr. Alkan's thesis, he said that lubricant imparts hydrophobicity; right?

A. He said that, but I did not review that paper.

Q. Let's turn to Bellantone I, please, in your binder. Are you there, sir?

A. Yes.

Q. That's an excerpt from Zydus' ANDA, it's called Quality Overall Summary. Do you see that?

A. Yes.
Q. Do you recognize it?
A. Yes.
Q. Because you reviewed it; right?
A. Yes.
Q. It was one of the materials that you considered for your expert report; right?
A. It was one of the materials, yes.
Q. Can you turn to -- there is page numbers on the bottom, sir, PTX 208.24. Actually -- I'm sorry, before you look at that page, I believe one of the criticisms that you had for Professor Hoag among others was the sourcing of the magnesium stearate excipient; right?
A. Yes.
Q. Now, on page PTX 208.24.
A. Yes.
Q. At the top you see there is a bullet called magnesium stearate?
A. Yes.
Q. Am I correct that Zydus represented to the FDA that no particular special grade is considered for this excipient?
A. It says that.
Q. That doesn't impact your opinion one way or the other?
A. No, it doesn't. And the reason that it doesn't --
Q. Sorry, sir, your counsel can redirect you with all

respect, I was just asking if it impacts your opinion.
A. Yeah, it does not change my opinion.
Q. So, with all the criticisms that you have of Professor Hoag's test, you can't really say one way or the other, though, whether those alleged differences make a difference on the penetration time?
A. Neither Dr. Hoag or I can say that it doesn't make a difference, that is correct, it's a reasonable question, however, that should have been considered.
Q. But you can't say for sure; right?
A. I will agree with that.
Q. Now, with respect to magnesium stearate -- I'm sorry, how long have you been working in the pharmaceutical industry for?
A. Well, as a pharmaceutical scientist, I started graduate school in 1983, and I have been a professor or in some form for twenty years. In terms of working in industry, I was never employed by industry, but I have consulted extensively for industry on real products.
Q. So ballpark, how many years have you been working in pharmaceuticals?
A. Consulting, really started probably around 2007 and you know for industry.
Q. And in your experience, have you ever heard of a nonhydrophobic magnesium stearate?

A. No. No.
Q. And so if we have a different source of magnesium stearate, I mean, at most all we're talking about are degrees of hydrophobicity; right?
A. No, not necessarily.
Q. You have never heard of a nonhydrophobic magnesium stearate?
A. That really doesn't mean that -- I mean, that's not directed question. All magnesium stearate is universally considered to be hydrophobic, yes.
Q. Now, you yourself have never performed a drop penetration test; correct?
A. That's correct.
Q. I assume you understand the test?
A. Yes.
Q. I think you have said in a deposition that you have supervised others performing drop penetration tests?
A. I believe that I said I thought that was more in context of either a Washburn or a wicking test. If I said that, it would have been misspoken. I believe that was in the context of either a Washburn or a wicking test which is the dissertation you were talking about.
Q. You have never supervised anybody conducting a drop penetration test?
A. That's correct.

Q. But you believe you would know how to perform one if you were asked; correct?
A. Yes. Yes, I do.
Q. And if you had to make the compacts like Professor Hoag did, you would know how to do it, I assume?
A. I am not a manufacturer, so I will not represent myself as having any expertise in running equipment or, you know, things of that nature. I mean, I do understand how things are done. I understand many things about the field in general, but in terms of if you want to turn me into a lab and have me -- I mean, certainly I can mix, but I don't know how to push the buttons or do anything of that nature, but I do understand the process of what's going on.
Q. I just want to be clear then, if somebody asked you yourself to make the compaction that Professor Hoag did, you would not be able to do it?
A. As a standing here or sitting here at this moment, I would not be able to go in and run the equipment.
Q. But you certainly know how to commission a lab to do it for you if you wanted to; right?
A. Sure.
Q. And so my question really is, whatever criticisms you have of Professor Hoag's test, source of API, source of magnesium stearate, bulk density, pore size, you could have commissioned a test yourself; right?

A. I could have commissioned a test myself, but I'm not sure I would have commissioned that test.

Q. If you wanted to reproduce Professor Hoag's test to see whether or not your criticisms were legitimate, you could have commissioned a test replicating Professor Hoag's test; right?

A. You just expanded your question. Let me answer both parts. If I wanted to exactly reproduce Dr. Hoag's test, assuming that it was exactly reproducible, I would commission a lab. However, if you could repeat the second part of your question, because if I wanted to say commission a test to reproduce say his results and conclusions, I would not be able to do that.

Q. You did not ask anyone to try to reproduce Professor Hoag's test; correct?

A. That was not what I was asked to do. That was not necessary for me to do to review what he did. My function was to review what he did and I don't have to go into a lab and verify that he weighed things correctly and so on. I accept his raw data, so no, I did not.

Q. But you didn't accept other aspects of his test, right, for example, pore size?

A. Well, there was no representation made of pore size. And that is one of my criticisms is that you are measuring one parameter, you are measuring just a time, but that time

is by all the theory, the equations that we didn't bring up, those equations say that there is one variable that you measure is time is a function of more than one possible cause, and he did not isolate and control the causes, and he is assuming everything is going towards lipophilicity, but he is not considering other aspects that are frankly even more likely related to pore size and so on.

Q. So my question is, you weren't curious enough to test your criticisms of Professor Hoag's test?

A. Well, I think that's an unfair characterization, because it's not about whether or not I'm curious, it's what was I asked to do. And had I thought that would be necessary to do, I might have mentioned that. I didn't think it was necessary to do to assess what Dr. Hoag had done.

And that, by the way, that's a universal practice. You don't have to reproduce somebody's results to understand what they attempted to do and how they interpreted their data, so no, I had no real curiosity to go and reproduce anything.

Q. You understand your counsel received samples; right?

A. I was informed that they received samples, yes.

Q. Am I correct also that actually you received some samples of certain materials; right?

A. That's incorrect, no.

Q. No, you didn't?
A. I did not receive any samples of anything.
Q. You know your counsel received samples.
The other case that you mentioned that you testified for here in Delaware --
A. Yes.
Q. -- do you remember that?
A. Yes.
Q. You performed a test for that case, didn't you?
A. Yes. What had happened in that case --
Q. I'm sorry, sir, respectfully it's yes or no. Did you perform a test in that case?
A. Yes, I did.
Q. So let's go to Dr. Bellantone's slide deck, DDX 11.21; please. Do you recall this slide where you were critiquing Professor Hoag's placement of the capillary?
A. Yes.
Q. And your position is that the capillary looks like it's askew; right?
A. Yes.
Q. You were in the courtroom, I can't remember if it was yesterday, I think it was yesterday or the day before when Professor Hoag testified; right?
A. Yes.
Q. Do you recall that he said that the angle of the

camera was looking down at the tablet?

A. I don't recall that particular statement. They have been looking and concentrating on that picture.

Q. I'll represent to you that's what he said.

A. Okay.

Q. In fact, actually you can tell that because you can see the top of the back of the tablet, so you can tell that the camera is not at the same eye level as the tablet; right?

A. Well, technically the answer is you're correct, but it's not exactly what I would consider an elevated enough view so I could get a detailed enough look at the surface so I could pick out any characteristics.

Q. Have you heard of the term "parallax error," p-a-r-a-l-l-a-x?

A. I know it extremely well. I'm a physicist.

Q. That word parallax is derived from a Greek word parallaxy which means alteration. Did you know that?

A. Okay. I don't speak Greek so I'll take your word for that.

Q. Do you know that concepts because of your physics background or because you do photography, how do you know that concept?

A. Physics.

Q. Can you turn to tab J in your binder. Do you see

there is an article here entitled How to Avoid Parallax Error in Your Proofs?

A. Yes.

Q. Under definition of parallax, it says parallax is an apparent difference or displacement in the position of an object when viewed along two different line of sights. Do you see that?

A. Yes.

Q. Is that generally consistent with your understanding of what a parallax error is?

A. Yes.

Q. Okay. Let's talk about Professor Hoag's results.

Now, in Professor Hoag's study, you agree that at least the way he conducted it, putting aside the differences that you have, okay. With respect to the data, you agree that there was a statistically significant difference in water penetration time between the mesalamine compacts versus the mesalamine plus magnesium stearate compacts; right?

A. I will agree that for the two blends or the two that he tested, and he did three replicates, he made, you know, one roller compacted material into a tablet, another roller compacted material into a tablet. I would agree for that one experiment and those replicates that the difference was statistically significant, yes.

Q. Thank you.

Now, let's look at your demonstrative DDX-11.27, please.

A. All right. Yes, I see that.

Q. All right. We just went over this a moment ago.

A. Yes.

Q. And you used this to illustrate that Professor Hoag's tests show that the mesalamine blend compact, meaning the one with magnesium stearate, is not lipophilic; is that correct?

A. That's correct.

Q. All right. I want to kind of do a process of elimination here, so first I'm going to ask you, often when you have hydrophilic polymers, they exhibit swelling in a pharmaceutical context; is that right?

A. When they are present, yes.

Q. And I'm correct that you did not see any swellable materials in Professor Hoag's compacts; is that right?

A. Right. These compacts were either pure mesalamine or mesalamine, colloidal silicon dioxide and magnesium stearate. No swellable components in there.

Q. In either compact?

A. Right. Right.

Q. Okay. And between magnesium stearate and colloidal silicon dioxide, magnesium stearate is the lipophilic

component of the two; is that right?

A. Yes.

Q. And when we're talking about pharmaceutical excipients, nothing is completely lipophilic. Am I right?

A. Yes, that's correct.

Q. And, in fact, if you had something, a pharmaceutical ingredient that had absolutely zero affinity for water in a pharmaceutical formulation, you would question its usefulness; is that right?

A. Well, actually, I think you are actually -- in my deposition, Mr. Saphia actually started to go down that road, kind of insinuating that I said that, and that you are actually quoting me, I believe. Yes. I never said that things were completely lipophilic and then I made that statement to corroborate that. You would never see a completely lipophilic excipient because it wouldn't be useful.

So that was the context. But, yes, I did say that.

Q. All right. I just want the record to be clear. You agree that if something had absolutely zero affinity for water in a pharmaceutical formulation, you would question the usefulness; right?

A. Yes.

Q. All right. And you agree that one possibility for the

resistance to the penetration of water in Professor Hoag's tests is because of the hydrophobicity of magnesium stearate; is that right?

A. Let me, let me give you a complete answer on that, if I may.

Q. Are you --

A. In the interests of doing proper science --

Q. I'm sorry. I just want to know if you can answer that question yes or no.

A. I would prefer to put it in a context that it would be, it would be one of the possible variables. Okay? But I don't want to give a sound bite where I'm just saying yes, because when you're properly doing science, you need to establish all of the possible causes in which ones you likely need to consider.

So I'm going to say, yes, that would be a possible one. Effects on compression and pore size would be another possible one. I'm not going to sit here not having done tests and choose one over the other. I'm not going to say that it could only be one. You have to look for both and you have to rule them both out. So it's possible, but in my opinion, it's not the likely one.

Q. Okay. And you did not do any tests of excluding other possibilities; is that right?

A. Well, that's why I'm not opining one way or another,

because I did not, and that would be doing exactly what I'm saying everybody else is -- it's kind of a confirmation bias here. People are seeing what they want to see, and I refuse to opine on something that I -- that I have not tested.

I need to be able to objectively rule things out, but I think it's an objectively valid concern, not controlling or characterizing pore size, because that is a very likely contributing factor.

Q. So I'm sorry. Within your answer you said you are not opining one way or the other; is that right?

A. That's correct.

MR. CHEN: No further questions, sir.

THE COURT: All right.

MR. CHEN: Thank you, Your Honor.

THE COURT: Redirect.

REDIRECT EXAMINATION

BY MR. GAERTNER:

Q. With me, Dr. Bellantone. A lot of documents here that are very thick and go through some of the ones that Mr. Chen did with you.

I would like you to first turn to Bellantone D, which is the Grove and Alkan article that Mr. Chen relied upon. Can you turn to that, please?

A. Yes.

Q. Okay. In particular, I think Mr. Chen, and I could be

wrong, again, I was juggling a lot of things, pointed you to the passage in the bottom left-hand column, where he talked about the field capillary when placed into contact with a tablet.

Do you see that? The first page, 575 of Bellantone Exhibit D.

A. Yes.

Q. Okay. Can you tell the Court what the size of the capillary was for that?

A. Let's see. Okay. I've got the page. Which --

Q. It's the last line on page 575.

A. Okay. Oh, okay. I'm sorry. The left-hand column. Right?

Q. Yes.

A. Yes. It was a two microliter capillary.

Q. Okay. So is that akin to a droplet?

A. Well, that would be, say, if you look at what was done, say, in the Hapgood reference, that was a six to eleven, so this would be even smaller than that.

Q. Okay. And, again, how much water did Dr. Hoag have in his capillary?

A. About almost 30 times. It was 57 that I calculated.

Q. Okay. So does this article, Bellantone Exhibit D, disclose the same method that Dr. Hoag used?

A. Well, there's some, you know, there are some

differences for sure, yes.

Q. And also if you could turn to Bellantone Exhibit E, which is the very lengthy Ph.D. thesis of Alkan. And if you can go to page 119 of Bellantone Exhibit D.

A. Exhibit?

THE COURT: Exhibit what?

MR. GAERTNER: I'm sorry. It's Bellantone Exhibit F. I'm sorry, Your Honor. Bellantone Exhibit F, which is the Ph.D. thesis.

THE WITNESS: Mm-hmm.

BY MR. GAERTNER:

Q. And page 119. Mr. Chen asked you to describe whether or not the exhibit, I'm sorry, the example, Figure 4.3, also disclosed Dr. Hoag's method. I would like to ask you, what type of instrument was used to disperse the water in Figure 4.3?

A. Yes. I apologize.

Q. Page 119.

A. Oh, okay.

Q. That's okay.

A. Sorry.

Q. Take your time. A lot of pages.

A. Misheard.

Q. All right.

A. Okay.

Q. Are you there?
A. Yes.
Q. All right. Figure 4.3, does that use a capillary?
A. Yes.
Q. Or does it use a micropipette?
A. That's correct.
Q. Okay. Does it use a micropipette?
A. Yes. In Figure 4.3, they used a micropipette.
Q. A micropipette would hold a lot less water than 57 microliters; is that correct?
A. It could hold much less, yes. That's why, that's -- that's actually what it's used for.
Q. Now, in that exhibit I think it's also helpful because it shows a cross-section of the tablet in which the water is penetrating; is that correct?
A. Yes.
Q. And does that illustrate the water penetrating through the spaces between the granules?
A. Yes.
Q. Mr. Chen also asked you a number of questions about pore size and things like that. I would like you to turn to the abstract of the same exhibit, Exhibit F, the Alkan thesis, if you could.
A. Okay. I'm there.
Q. And in the first, I'm sorry, the first sentence of the

second full paragraph, it reads:

"In order to provide a complete analysis of factors involved, it became necessary to determine the size of the voids or pores in the compact."

Do you see that?

A. Yes, I do.

Q. And Dr. Hoag did not do that; is that correct?

A. That's correct.

Q. And in this case the scientists actually used a low pressure gas permeability technique to measure the pore size; is that correct?

A. That's correct.

Q. Did Dr. Hoag do that?

A. No, he did not.

Q. To page 21 of the same reference, again, relating to questions about pore size. And I am referring to Bellantone F.

Are you there, Dr. Bellantone?

A. Yes.

Q. And on page 21, under the heading 1.2.3, it's reads: "Compressional force can affect the disintegration time by firstly reducing the pore space and decreasing the penetration of liquid into the tablet.

"And, secondly, by breaking down the granules and causing the internal starch, which is the ingredient

there, to be more effective."

Do you see that?

A. Yes, I do.

Q. Again, you testified that Dr. Hoag did not measure the compressional force that he used to compress his blended tablet?

A. That's correct.

Q. And is that consistent with your testimony that compressional force can affect pore size, shape and morphology?

A. Yes, it is.

Q. All right. Mr. Chen also asked you a number of questions about the differences that the ingredient in manufacturing process could be and could give rise to. I would like you to turn to page 24 of the same document. That's Bellantone Exhibit F?

A. Yes.

Q. Section 1.3. Are you there?

A. Yes, I am.

Q. And just under Section 1.3, the author wrote, "The physical properties of compressed tablet depend mainly on the properties of the components, the formulation, and the manufacturing process."

Is that correct?

A. Yes.

Q. And at one point, Mr. Chen interrupted you when you were trying to explain your answer about -- excuse me -- a statement in the Zydus QOS to the effect, just quoting what my notes were, so don't take this literally. "No particular special grade is considered for this excipient."

Do you remember that?

A. Yes.

Q. All right. Could you please explain your answer?

A. Well, there, they're saying there's no particular grade. However, you know, even within a grade, there can be variations, and certainly, there can be differences supplier to supplier within the same grade. We had discussed some of that. So that statement does not eliminate any differences or inconsistencies in the materials that should have been used in Dr. Hoag's test.

Q. And again is it, remains your opinion, Dr. Bellantone, that Dr. Hoag did not control for the many variables that we discussed this morning such that you can draw scientifically reliable conclusion about the effect of magnesium stearate?

A. Yes, in particular, with his penetration time, that there are things that he didn't control for including the pore size distribution as well as any possible lipophilicity that he was trying to get at. My point there was if you don't control for those, you can't draw conclusion which is actually one of the reasons I looked at the extent of the

penetration as an alternative objective measure because in my opinion having that control, his penetration times really don't tell you anything.

I think it's more likely that it's pore size given the amounts of materials, but I can't say that for sure which is why I turned to the extent and the amount of the water taken up, because he did have enough information to make a determination, that's another objective measure.

MR. GAERTNER: I have got nothing further, Your Honor.

THE COURT: Thanks. Mr. Bellantone, you may step down. Let me ask the court reporters how are you doing?

Your next witness, Mr. Gaertner.

MR. GAERTNER: Your Honor, before I move in, I'll give a copy to the clerk and the plaintiff, I designated the screen shots that are moved into evidence DTX numbers. So we have DTX 1008 is going to be the still shot on DDX 11.20 which is the Hoag video at 03 -- three minutes and two seconds; PTX 581 and DTX 1009 is DDX 1121, Hoag video, three minutes two seconds PTX 580. I'll pass these up on the break but I just want to read these in.

MR. CHEN: No objection.

THE COURT: Thank you, Mr. Chen. Those were matters to be admitted or those were matters just to be.

MR. GAERTNER: Mr. Chen had already allowed me to admit them, when I said Judge, we need the still shots I was going to assign the DTX.

THE COURT: So it's just the number?

MR. GAERTNER: Yes, sir.

THE COURT: I understand. Thank you. Who is your next witness.

MR. ABRAMOWITZ: Your Honor, Dave Abramowitz for Zydus. We are going to call Dr. Mark Sacchetti, who is the -- who performed the DSC and hot-stage testing for Zydus.

... MARK JOSEPH SACCHETTI, having first duly sworn as a witness, was examined and testified as follows ...

MR. ABRAMOWITZ: Your Honor, if I may approach.

THE COURT: You may.

DIRECT EXAMINATION

BY MR. ABRAMOWITZ:

Q. Good morning, Dr. Sacchetti. Can you please state your full name for the record.

A. Mark Joseph Sacchetti.

Q. What's your current position?

A. I'm scientific director of the Zeeh Pharmaceutical Experimental Station.

Q. Could you briefly summarize your academic background for the Court since high school?

A. I obtained a bachelors degree in chemistry with honors from Temple University in 1987. I obtained my masters and Ph.D. degrees at University of Wisconsin in pharmaceutics in 1990 and '92.

Q. After you finished your Ph.D., did you obtain some professional experience?

A. Yes.

Q. Can you explain your professional experience for the Court?

A. I worked in the pharmaceutical industry for approximately fourteen years, mostly at GlaxoSmithKline and its predecessor companies. My work involved evaluating physical chemical properties of new drug candidates and other materials. For example, I have used techniques relevant to this case such as x-ray, powder x-ray diffraction, differential scanning calorimetry, thermographic microscopy, other techniques that are listed in my CV. Either myself or somebody in any group was responsible for developing and validating methods and transferring them to manufacturing sites for cases where products, which physical chemical properties were a critical factor.

In 2007 I left and came to the University of Wisconsin to my current position as the scientific director. The station is a consulting and contract lab organization, the

school of pharmacy. We mainly work with private pharma companies but also helping university professors advance their drug discoveries.

Most of the work I do is in the area of physical chemical properties, but we also do other types of experiment, and I also have teaching responsibilities, in particular I teach continuing education courses in drug development pertaining to physical chemical property.

Q. And do your duties and your composition including teaching and supervising the DSC and hot-stage techniques?

A. Yes.

Q. If you look in your binder at DTX 101, that is a true and accurate copy of your CV?

A. Yes, with just some minor updates since this time.

Q. And is it -- is the DTX 101 an accurate summary of your academic professional achievements and experience to this point?

A. Yes.

MR. ABRAMOWITZ: Your Honor, we offer Dr. Sacchetti as an expert in solid state chemistry and solid state chemical testing.

MR. LIEF: That's fine, Your Honor. I note I don't think I have this in my binder. We don't object to the exhibit or him as an expert as described.

THE COURT: All right. We'll hear him as an

expert and there is a copy of the binder with the CV in it if you would like to see it.

Go ahead, Mr. Abramowitz.

BY MR. ABRAMOWITZ:

Q. Dr. Sacchetti, what were you asked to do in this case?

A. I was asked to run DSC and hot-stage microscopy in a sample of magnesium stearate.

MR. ABRAMOWITZ: We offer DTX 101, the CV into evidence.

MR. LIEF: No objection.

THE COURT: It's not objected to so it's admitted without objection.

BY MR. ABRAMOWITZ:

Q. Do you a declaration in the case that explained the work that you worked in and supervise the station?

A. Yes, I did.

Q. Is DTX 100 a true and accurate copy of that declaration?

A. Yes, it is.

Q. Was the magnesium stearate sample that you received on batch 0908123024?

A. Yes.

Q. And can you explain to the Court how this testing was conducted?

A. DSC testing?

Q. The DSC testing.
A. Yes. It was done by weighing a specific amount, 1.4 milligrams into a PSP pan which was then added into the equipment. The sample was heated at a prescribed rate, 500 degrees Celsius from a prescribed starting to a final temperature.
Q. Were you present during the DSC experiment?
A. Yes, I was, other than not watching the exact weighing of the sample but I looked at the sample weight record in the notebook as well as what was in the software.
Q. Was the experiment conducted under your supervision?
A. Yes.
Q. Looking at DTX 102 in your binder, are those true and accurate copies of the results of your DSC experiment?
A. 102, yes.
Q. And can you explain just briefly what the numbers on DTX 102 represent?
A. There is three numbers, an onset temperature which is the extrapolated value of that straight line. There is a peak temperature and then there is a heat value.
Q. And which one is the onset value?
A. The onset is the one that's close to where you see the extrapolated line, so, for example, for the first peek, the 73.89 Celsius, the second peak is 125.56 Celsius.
Q. Which one is the peak value?

A. The peak value is the one listed at the peak which is the minimum in this case, 87.61 degrees Celsius and 127.73 degrees Celsius.

Q. How are these values calculated?

A. The person doing the analysis simply establishes the range as you see there, the beginning and the end of the peak and the software has an algorithm and calculates the values.

Q. Was the DSC machine used to conduct the experiments calibrated?

A. Yes, we run an Indium standard.

MR. ABRAMOWITZ: Your Honor, we offer DTX 102 into evidence.

MR. LIEF: No objection.

THE COURT: It's admitted without objection.

BY MR. ABRAMOWITZ:

Q. Now, what about your hot-stage microscopy, can you explain to the Court what a hot-stage microscopy experiment is?

A. In hot stage a very small sample is spread on a glass cover slip for the purpose of hot stage is sandwiched between a second cover such that you produce a nice flat specimen. That's inserted into the hot stage unit, which simply is a heating stage. And then that whole unit is placed on a microscope, and then the person doing the

analysis would bring the sample into focus and set the program to scan up the heating rate of the hot stage.

Q. Were the hot stage experiments you conducted, how many -- first how many hot stage experiments did you conduct?

A. A total of four replicates.

Q. And were they conducted in the same batch of magnesium stearate as the DSC?

A. Yes.

Q. Could you explain to the Court what exactly went on in the hot stage experiment for the setup and process?

A. I think we have a demonstrative.

Q. Do you want me to put up the demonstratives to help with that?

A. Yes. So this slide is showing 30 to 80 degrees Celsius for one of the samples.

THE COURT: Get on the record what slide we're looking at.

Q. DDX 5.3 and go through 5.4 and 5.5.

A. Okay. So these images just capture what the sample looked like over the temperature range and there is no observed changes. Moved on to the next one. Likewise from the temperature range on DDX 5.4 we have no change in appearance from 88 to 93 degrees Celsius.

Q. Next slide, please.

A. And on the next slide, DDX 5.5, where we start to see some changes, and most notably they occur starting at about 130 degrees Celsius where the samples appear to brighten and some changes in some shape and features.

Q. Now, are DTX 103 and 104 true and accurate copies of the still photographs you took of the thermoscopy experiments?

A. Yes.

MR. ABRAMOWITZ: We move DTX 103 and 104 into evidence.

THE COURT: Which are you moving into evidence?

MR. BLEIBEL: DTX 103 which is appendix 2 from Dr. Sacchetti's declaration and DTX 104 which is a separate binder we handed you, which is a big set, essentially a hundred images.

MR. LIEF: No objection.

THE COURT: Admitted without objection.

BY MR. ABRAMOWITZ:

Q. In setting up your hot stage experiments, did you also use video to record your results?

A. Yes, two of the samples a video was captured.

Q. Could we see DDX 5.6. Can you explain to the Court what's going on in DTX 5.6?

A. This is an image of a second sample, and the thermometer on the left is illustrating the rise in

temperature. You can see occasionally the sample is sliding a bit, and there is an occasional refocusing that is done and it's very typical for this measurement, it's hard to keep it steady.

Overall the main feature are no changes are observed in this video, even up to the point which is about a hundred degrees Celsius. You start to notice them when the temperature gets up to about 130 or so, you start to see the brightening, and ultimately you'll see at some higher temperature the presence of liquid.

Q. And the video that we played is DTX 105; is that correct?

A. I don't actually have in my copy an actual picture, but if that's what it says on the slide, yes.

MR. ABRAMOWITZ: We admit DTX 105 into evidence.

MR. LIEF: No objection.

THE COURT: Admitted without objection.

BY MR. ABRAMOWITZ:

Q. Can you explain a little more for the Court why the camera sort of moves a little bit while the sample is being tested?

A. Well, the cover slip is being heated and it's very difficult to keep it totally steady, you have to bear in mind that the sliding that we're seeing is only on the order of ten or so microns, about the width of a human hair, so

it's difficult to really keep it steadier than that.

Q. Did you run any standards to assess whether your hot stage microscope was calibrated?

A. Yes, we do a benzoic acid melt.

Q. What was the result of that testing?

A. That was, I think we saw a range that's in my declaration of 122 to 123.5, and the value is 122.43 Celsius.

Q. Were you asked to analyze the results of your DSC and hot stage testing any further?

A. No.

MR. ABRAMOWITZ: No further questions.

THE COURT: Okay. Cross-examination, Mr. Lief. You may proceed.

CROSS-EXAMINATION

BY MR. LIEF:

Q. Good morning, Dr. Sacchetti.

A. Good morning.

Q. Am I correct that your Ph.D. was not about melting?

A. That's correct.

Q. And am I also correct that you have never published on the melting of magnesium stearate?

A. That's correct.

Q. You have never published on the melting of a hydrate, either; is that correct?

A. Possible, I can't say that for sure without looking at my publications.

Q. You have never observed the melting of a hydrate in your career; correct?

A. Yeah, I think it's -- well, I have seen it in at least one or two literature publications the melting of a hydrate, but I haven't actually observed that with any hydrate that I have worked with.

Q. You have never personally observed that in the lab?

A. That's correct.

Q. And in terms of the experiments you did, am I correct that you followed written protocols that were given to you by your lawyers; is that correct?

A. Correct.

Q. And in terms of experiments that you didn't do, in your direct I believe you mentioned you're familiar with XRPD, x-ray powder diffraction experiments, you know how to do that; correct?

A. Yes.

Q. You didn't do those experiments on this sample; correct?

A. No.

Q. Am I correct that you undertook no study of anisotropy of this sample?

A. No.

Q. Otherwise known as birefringence, no birefringence studies; correct?
A. Correct.
Q. That's normally done on a setup that's a microscope like that?
A. I wouldn't say normally done, but it can be done.
Q. Can be done. You didn't do a thermogravimetric analysis here, either; is that correct?
A. No.
Q. When you tested your sample, you ramped the temperature up, am I correct that you never went up and down, up and down with the temperature?
A. That's correct.
Q. You never cooled the sample, in other words?
A. That's correct.
Q. You agree that liquids do not show anisotropy?
MR. ABRAMOWITZ: Objection, Your Honor. This is beyond the scope. Dr. Sacchetti simply reported the results of his testing.
THE COURT: I'm not sure how that goes to anything he testified about.
MR. LIEF: Withdrawn.
BY MR. LIEF:
Q. Am I also correct that your experiments don't establish one way or another whether the Zydus magnesium

stearate product is a channel hydrate?

MR. ABRAMOWITZ: Objection. The doctor testified he didn't do any --

THE COURT: That's not outside the scope, he's just asking whether he did it or not. I'll let him answer that question, if I understood the question properly.

THE WITNESS: Could you ask it again.

BY MR. LIEF:

Q. Your experiments did not establish or determine one way or another whether the Zydus magnesium stearate is a channel hydrate; correct?

A. There is no experiment other than what I have reported, DSC and hot stage.

Q. The visual method of determining melting point, would you agree with me that that is the old fashioned method of doing it; isn't that right?

A. No.

Q. You don't agree with that?

A. No.

Q. In your cross-examination binder, I believe it is Tab 12, you have a deposition -- you have your deposition from 2012, do you see that?

A. Did you say Tab 12?

THE COURT: It's a little out of order, Doctor, if yours is like mine, it goes from 10 to 17 and then

descends to 12.

MR. LIEF: Sorry about that.

THE COURT: Then maybe it's in there upside down. Maybe I have got the binder upside down. I don't know.

THE WITNESS: So in Tab 10 I see, I see a trend, in Tab 10.

BY MR. LIEF:

Q. In Tab 10 you have your 2012 deposition?

A. I'm sorry, no, this is for someone else, so it's not testimony.

THE COURT: At Tab 12 I have the videotape deposition of Thomas V. O'Halloran.

THE WITNESS: I do as well. We have been given someone else's.

MR. LIEF: Actually my mistake. I apologize. This is O'Halloran's 2012 deposition. Tab 12. Do you have that?

THE WITNESS: That is what I'm supposed to have okay.

Q. All right. I apologize.

A. Oh, it's not tab 12. I think it's tab 10 then.

THE COURT: There's also one at tab 12. The one at tab 10 is 114.

MR. ABRAMOWITZ: Objection, Your Honor.

He can't be cross-examination him on someone else's deposition.

THE COURT: I am a little curious we're you're going with this, Mr. Lief. What is in Mr. or Dr. O'Halloran's deposition that is going to be relevant cross-examination here?

MR. LIEF: You know, it is the concept that this is an old-fashioned test, but we can --

THE COURT: So you can ask him questions about that and he'll give you his answer, but I'm not sure where you go with somebody else's deposition.

MR. LIEF: All right. Let me move on.

BY MR. LIEF:

Q. In your experimentation -- let me ask you a more general question.

Would you agree with me that in the general way, that there are things that we know exist in the world that we cannot see?

A. That's a very general question.

Q. It is.

A. I'm not really sure what to make of that.

Q. Well --

A. Can you be more specific?

Q. As you and I look at each other right here across the courtroom, would you agree with me that there are

infrared beams bouncing around in front of us that we can't see?

MR. ABRAMOWITZ: Objection, Your Honor. I don't know where this is going.

THE COURT: I don't know where it's going either, Mr. Abramowitz, but I'm prepared to let him go for a while.

It's not like cross-examining with somebody else else's deposition. Give him some leeway. You can sit down and he can talk and we'll see where it goes.

Go ahead.

THE WITNESS: Well, I think it's such a general question that I can't say anything other than there are certain, like electromagnetic radiation, as you point out, and atoms and molecules that we can't see by eye, correct.

BY MR. LIEF:

Q. And in terms of the experiment you did, am I correct that, in your view -- you watched the experiment you did with your own eyes; is that correct?

A. The hot stage is watched through a magnifying glass, so it's not just with my own eyes.

Q. Well, but you personally witnessed it; is that correct?

A. That's correct.

Q. All right. And am I correct that having witnessed it, your observations, you did see at some point in that experiment magnesium stearate turn to liquid; is that correct?

A. Correct.

Q. And when you saw it turn to liquid, am I correct you saw it as a viscous material; correct?

A. Yes. It -- it certainly demonstrates that -- so what we first see, and as I put in my deposition, there's evidence that some liquid is forming as low as about 130 degrees Celsius, but that the gross appearance of a liquid does not occur until that much higher temperature of 145 or 150 degrees Celsius, which is indicative it's a fairly viscous material.

Q. It's a viscous material when it melts and it's difficult to see; is that correct?

A. It's difficult to see. We can see it at the 130 degrees Celsius, you can see the first evidence for it.

Q. But -- well, let me talk to you about that, because I think that's a very interesting number, 130.

If we look at your DSC experiment -- can we look at that? That is in your report. I believe it is -- I'm hoping my tabs are right. Tab 1 in your report, in your book.

A. Oh.

Q. No, not tab 1. I'm sorry. Tab 2. And if we could look at page 6 of your report. This is your DSC, correct, on page 6?

Do you see that?

A. Yes.

Q. And the onset that you report for the second peak is at 125; is that correct?

A. Yes.

Q. Okay. And am I correct that onset is representative of melting in DSC; is that correct?

A. Well, it's representative of an onset of what's occurring, whether it's melting or not.

Q. And you understand there's a melt going on at 120 or above; is that correct?

MR. ABRAMOWITZ: Objection, Your Honor.

Dr. Sacchetti was not asked to analyze the DSC results. Mr. Lief is asking him to analyze materials for which he has not provided materials on either in his declaration or during his direct.

THE COURT: Let me have the question again.

BY MR. LIEF:

Q. You understand that there was a formation --

THE COURT: Hold on. Mr. Lief, I'm sorry. I wasn't clear. When I said let me have the question again, I mean from the court reporter. I apologize.

(The court reporter read back the question as follows:

"Question: And you understand there's a melt going on at 120 or above; is that correct?")

THE COURT: All right. Removing your objection. He has already talked about what he saw, called it a melt. Go ahead.

BY MR. LIEF:

Q. All right. If you could answer that.

A. The question is? Just what was read?

What -- the DSC in itself doesn't tell us that it's melting. The hot stage microscopy result is where I'm saying it's about 130 degrees Celsius is the first evidence for melting.

Q. The DSC shows an onset earlier than that; is that correct?

A. It -- the event that we're looking at in DSC is occurring over a fairly broad range, as you can see.

Q. You think the first, you think the second peak is a fairly broad range. Is that your testimony?

A. No. I'm referring to the whole range that is highlighted there with the beginning marking and end marking.

Q. So you're saying from 70 something up to 130-something?

A. No. My apologies. The second peak right there (indicating). All right. This is the DSC event. What we're actually seeing in the hot stage microscopy is just towards around the maximum of that event. That's where we're actually starting to see some particle changes that are indicative of the beginning of melting.

Q. All right. The DSC shows an onset around 125; is that correct? That second peak?

A. Yes.

Q. Okay. And if we could look at, I believe it's tab 6 in your book, the 125 picture or run 2, which I believe you showed.

This is 30. If we could look at 125. Am I correct that here, there's no liquid visible; is that correct?

A. If you -- if you tab -- that's correct. If you tab --

Q. Thank you. That was the answer.

A. Oh.

Q. Thank you.

Now, I believe you also said that you saw no changes from 30 up to maybe 130, was that your testimony, in visual inspection?

A. Yes. I would say even maybe more like 30 to 120 degrees Celsius. I think there are -- there's some

evidence of some brightening that occurs starting as early as 120 to 130.

Q. Now, is it correct, Dr. Sacchetti, at 85 to 86 degrees in your visual inspection, there was a loss of focus in the picture? Yes or no?

A. I'd have to look at that.

Q. Why don't we take a look at your deposition, which I believe is tab 1, at page 112. And at line 6, there's a question:

"Question: Okay. Similarly, if you can take a look at Exhibit 3, which was run number 1 (sic) and if you look at the 85-degree picture and the 86-degree picture.

"Answer: I'd say it looks like a point where refocusing may have been done. If you look at it, especially from 30, it was in pretty good focus, but as it was heating it looks like, you know, it lost some focus, and so at that point it looks like the focusing mechanism was moved a bit to put -- try to improve the image.

"I mean, the idea is to get the best image possible, and if it's losing focus, we'll adjust the focus."

Were you asked those questions and did you give those answers under oath?

A. That's correct.

Q. Okay. Thank you.

A. So --

THE COURT: Let me just make one correction. I think you misread and said run number one. It's run number two according to the transcript.

MR. LIEF: I apologize. I thought I said run number two.

THE COURT: Go ahead.

BY MR. LIEF:

Q. And am I correct that you did not consider why it was that you lost focus at 85 to 86 degrees; is that correct?

A. We lose focus from time to time throughout, some samples more than others. It's a fairly random event. It quite literally could have been a door closing, and this always occurs with every sample that I've ever done in microscopy, and the fact that, at whatever temperature I just attribute that to it does happen. We need to actually refocus it from time to time.

Q. The fact of the matter is, you did not consider why you lost focus at that temperature, is that correct, when it was being heated?

A. I didn't, because --

Q. Thank you.

And you have no idea why during heating at 85 to 86, you would have lost focus; isn't that right?

A. For the very same reason I have no idea at other temperatures.
Q. Okay. But you saw it lost the focus -- coming up from 30, you saw it at 85 to 86?
A. And we see it at other temperatures as well.
Q. But you did not see it from 30 to 85; right? That was your testimony?
A. I think if you look at that, we may actually see, if we go through it carefully, there's a gradual loss of focus an it's not something that occurs very abruptly.
Q. Okay.
A. It was 85 to 86 that the focus was changed, because at that point, it had gone out of focus sufficiently. It seemed necessary to change it.
Q. Did you take, undertake any investigation of why at 85 to 86, in particular, you needed to refocus because it had lost focus?
A. There's nothing special about 85 to 86. It was just gradually losing focus.
Q. All right. Am I also correct that 85 to 86 is after the first onset of the first endotherm in the DSC; is that correct?
A. I think that's correct in terms of where the endotherm is located.
Q. And it's, in fact, within that endotherm; is that

right?

A. If we can pull up the DSC.

MR. LIEF: If we could look at that.

BY MR. LIEF:

Q. 85 to 86 is within that first endotherm; correct? And it is after the onset; is that correct?

A. Yes.

Q. Thank you.

Now, amongst the things you also did not see in that first endotherm and that first temperature range: did you see any water leave the sample?

A. No.

Q. Okay. Now, do you rule out the possibility that there was a melt in this first endotherm in your opinion?

A. Well, I have not looked at the literature, and I've not been asked to look at the, any of the evidence and so forth for this case, but I did have, as I said in my deposition, general knowledge of an interpretation of that, that first endotherm and the scientific literature.

Q. All right.

A. And from what I've seen, that first endotherm is only referred to as dehydration. I have not ever seen any of the literature, and I think I've said it here, that said there was a melt involved in that.

Q. You are unaware of that literature?

A. That's correct. Well, the literature that I know.
Q. Okay. Thank you.
A. I never --
MR. ABRAMOWITZ: Objection, your Honor. Dr. Sacchetti is not being offered as an expert.
MR. LIEF: That's fine.
THE COURT: Wait a second, Mr. Lief. I've got an objection and I'm thinking about it for a second, and I guess what I hear you saying is you're moving on. You are not going to ask any more about it.
MR. LIEF: I think that's -- he said he's not, he's not addressing it and he hasn't seen that literature. I think that was the answer.
THE COURT: All right. Okay.
BY MR. LIEF:
Q. All right. And, again, with respect to DSC, you do agree that when you take a DSC, the most common report for the melting point from a DSC is the onset; is that correct?
A. I think that's probably right. If we go off and see both the onset and peak, it is probably emphasized, the onset.
Q. It is correct that the onset is considered the most representative for melting; is that correct?
A. I'm not sure I've actually given any real thought to that, if that should be correct or not, to say that's the

most representative. The reason I say that is the onset also reflects the presence of, for example, chemical impurity and can be lowered by chemical impurity, so there could be -- certainly, there are cases where the onset may not be the best temperature to actually represent the melting of a pure material.

Q. If you could look at your deposition again, which is tab 1, at page 46, at line 3, through about line 20.

"Question: And to your understanding, would the onset point in DSC be the point at which for melting purposes, liquefaction begins?"

There was an objection. And you answered:

"You know, again, this is just general knowledge of -- of DSC, but the idea is that melting begins earlier on in -- in that phase, and that the onset is considered more representative melting for that reason."

MR. ABRAMOWITZ: Objection, Your Honor. I don't this is impeachment. His question was about melting point, not about a fact dispute. Your claim construction separates out those two particular aspects of the process.

THE COURT: Well, I'm not sure at all, Mr. Abramowitz, what the claim construction has to do with this exchange. I understand your objection at the time, but if your objection is that the claim construction obviates this question and answer, that is overruled.

MR. ABRAMOWITZ: I assumed the original question was about melting point. This is about liquefaction. It's outside the scope of his direct testimony, and this is asking for an opinion on melting point.

THE COURT: Well, that objection I will sustain. It was good at the time of the deposition. I think it's probably still good now, Mr. Lief.

BY MR. LIEF:

Q. Would you agree in terms of a visual analysis of hot stage, that a localized melt is difficult to see?

A. Localized melt? I guess I'm not quite sure what that means other than you're referring to just maybe the beginning of melting?

Q. Not the beginning of melting. I'm talking about the presence of a small amount of liquid in a small local area. That's difficult to see, isn't it?

A. Well, it certainly depends on the -- it depends on the material. If you had a -- if you had a, let's say a larger crystal, you might be able to see that quite readily.

Q. Crystals you examine, were they big crystals or little?

A. I'm just saying --

Q. Well, my question is, were they big or little?

A. For magnesium stearate that we're looking at, they're small.

Q. Thank you.

Now, do you agree or do you not agree that small localized melts are difficult to see visually?

A. If it's beyond, if it's a small particle and beyond the limit of your magnification, sure, then you wouldn't be able to see it.

Q. And would you also agree that if there's a rapid recrystallization of a liquid taking place, then the presence of the liquid to be seen visually could be fleeting?

MR. ABRAMOWITZ: Objection once again. Outside the scope of the report.

THE COURT: Overruled.

MR. ABRAMOWITZ: And asked.

THE WITNESS: If the recrystallization involves a change or appearance of new particles that have grown out of that, then that could be seen.

BY MR. LIEF:

Q. Well, I'm talking about seeing the liquid. If you have a liquid that forms and then rapidly recrystallizes, that could be something that is fleeting and difficult to see; right?

A. But I'm saying if it recrystallizes, you could end up seeing the appearance of a tiny crystal.

Q. That is not my question, although we may come to

that.

THE COURT: Don't interrupt him. Let him finish, and then if you think he's not answer answering it, go ahead.

But go ahead, Doctor.

THE WITNESS: You're saying if it's a little bit of liquid form and it recrystallizes, you may not see the liquid, but you'll see the crystal reform.

BY MR. LIEF:

Q. And you agree that the liquid itself, the appearance of the liquid could be fleeting?

A. Sure. I mean, it could be a fast thing.

Q. Again, you've talked about 130 is where you started to see visually evidence of liquid; is that correct?

A. Yes.

Q. Now, someone else actually ran the experiment. You were present, but there was a technician who ran the experiment; is that correct?

A. I was right there sitting beside them.

Q. And the lab notebooks, did you write the lab notebooks up or did your technician write them?

A. Technician person.

Q. All right. And am I correct that in the lab notebooks, even at 130, there was no written statement of melt or liquid?

A. Can I -- can I see that? I think we have the lab notebook.

Q. Why don't we look at your deposition at page 135. This is tab 1.

A. Well, I just thought that there is, there is a statement made in the lab notebook and we should look at that.

MR. ABRAMOWITZ: Objection, Your Honor. If he was provided the lab notebook at his deposition. If it's for impeachment, it's unfair.

THE COURT: I don't think it's unfair, Mr. Abramowitz, and you can, you can redirect him if you want.

He can ask him questions from the deposition. If you want to show him the lab notebook on redirect, do it. Mr. Lief has got the podium. Go ahead.

BY MR. LIEF:

Q. If we look at 135 of your deposition at around lines 15 through 21, the question, "Am I correct that she does not report in that sentence that she visually saw liquid form between 120 and 130; correct?

"Answer: The words certainly don't -- well, the words say "melt," and -- I think as I discussed earlier, you don't necessarily see a bulk liquid forming at the melt if it's a very viscous material."

Did I read that correctly.

A. Yes, you did.

Q. And that was your testimony; correct?

A. Yes.

Q. And again, magnesium stearate when it -- to the extent it forms a liquid, it forms a very viscous material; right?

A. It appears to be the case at this temperature, yes.

Q. And those viscous materials are difficult to see; correct?

A. Well, we did see it.

Q. Eventually you did?

A. We saw it at 130. And the person didn't use the word melt.

Q. You didn't see it at 125; right?

A. I think the very first images are just higher than that, it's very close to the peak, peak value of the 127 or 128 value.

Q. Can we take a look at the 130 picture for a moment. First of all, it's a little blurry there, isn't it?

A. It's a difficult material to image, yeah.

Q. Difficult material to image. Thank you.

MR. LIEF: No further questions.

THE COURT: No question pending, Doctor. Your redirect.

REDIRECT EXAMINATION

BY MR. ABRAMOWITZ:

Q. Dr. Sacchetti, counsel just cut you off. Can you finish your answer to his question?

A. What we need to do is look at the images in series starting from about 125 through 130 or so and you will see that the images change and there is evidence that the particles are starting to undergo some change in that range. If you have the other one --

THE COURT: Hold on a second. It's kind of structured formally. You have to wait until he ask the question and then you can respond.

BY MR. ABRAMOWITZ:

Q. Dr. Sacchetti, could you walk the Court through what happened from 125 to 130 using the images in DTX 104?

A. If one scans through the images and see them as one after the other, you can start to see some of the changes. Here you go.

Q. And what --

THE COURT: Hold on just a second because I want the record to reflect. When you say there you go, at what point in that scan did that happen?

Q. At the 127 slide when you said there you go, what did you see?

A. You can see some movement of the particles and change in the image, and that was at 127; correct?

Q. Yes.

Now, during cross, Mr. Lief discussed refocusing at 85 to 86 and you didn't really complete your answer about why it may have refocused on 85 to 86. Can you explain to the Court what happens in refocusing?

A. As I said, overall as the sample was heated, it was losing focus. The fact that it fell -- that we refocused it at 85 to 86 it was a gradual process leading up to that, it didn't reflect any event that occurred at that point.

Q. I believe you testified earlier you ran multiple replicates of these tests; is that correct?

A. That's correct.

Q. If we look at DTX 104 run one at the two images at 85 and 86, did you see a refocus?

A. We can look at it. As I said, it's more of a random thing.

Q. We're looking at the 85 which is DTX 104, and can we see 86. Was there a refocus there?

A. No.

Q. So when slides go out of focus due to any number of things. Is that a random occurrence?

A. Yes.

Q. So you wouldn't attribute any particular import or not to the fact that the slide went out of focus, or was refocused at between 85 and 86 in run two?

MR. LIEF: Objection. Leading.

MR. ABRAMOWITZ: I'll withdraw.

THE COURT: Yes. And he said it and I have heard it, so I believe the point that you're endeavoring to make has been made, so you can go ahead.

MR. ABRAMOWITZ: Okay.

BY MR. ABRAMOWITZ:

Q. If we could go back to run two and start at about 75 mil, 75 degrees C, I believe Mr. Lief cut you off. You were testifying earlier about how during the loss of focus it happens gradually. Could you walk the Court through from 75 to 85 and show what happens?

A. Okay. The images are advanced.

Q. Look at 75. Now 76. Now 77. What's happened at 77?

A. There is just some slight movement of the particles that occurs.

Q. 78, 79?

A. Right.

Q. 80. 81. 82. 83. 84. 85. Now 86, in looking in that series, did you see any change to the particles?

A. No.

Q. Was the only change -- what change did you see?

A. Other than at 86, it was judged that it was time to refocus, so that's what happened.

MR. ABRAMOWITZ: I have no further questions.

THE COURT: Thank you. Doctor, you may step

down. Thank you very much.

All right. We'll go ahead and take our lunch break right now. I'll see you back here at 1:30. Okay. Thanks.

(Witness excused.)

(A luncheon recess was taken.)

Afternoon Session, 1:30 p.m.

THE COURT: Thanks. Please be seated.

MR. ABRAMOWITZ: Your Honor, we're going to call our next witness. This is Zydus' melting point expert actually.

THE COURT: All right.

MR. ABRAMOWITZ: Dr. Mark Hollingsworth.

THE COURT: All right.

... MARK DAVID HOLLINGSWORTH, having been duly sworn as a witness, was examined and testified as follows ...

MR. ABRAMOWITZ: Your Honor, if I may approach with some binders?

THE COURT: You may. Thank you.

(Mr. Abramowitz handed binders to the Court.)

THE COURT: Please proceed.

DIRECT EXAMINATION

BY MR. ABRAMOWITZ:

Q. Good afternoon, Dr. Hollingsworth.

A. Good afternoon.

Q. Could you please state your full name for the record?
A. Mark David Hollingsworth.
Q. Could you provide the Court with your current position?
A. Yes. I'm an associate professor of chemistry at Kansas State University.
Q. And before you became an associate professor at Kansas State University, can you give the Court sort of a brief summary of your academic experience after high school?
A. Yes. I got -- had my B.A. in chemistry from Carlton College and then I went on to do my Ph.D. in chemistry at Yale University. After that, I was a NATO post-doctoral fellow at the University of Cambridge in the U.K.
Q. What was the subject of your Ph.D. dissertation?
A. My Ph.D. dissertation focused on reactions in organic crystals.
Q. And did you receive any awards or honors for your Ph.D. dissertation?
A. Yes. The two main ones were the Nobel Laureate Signature Award for Graduate Education in Chemistry from the American Chemical Society, so that honors the most distinguished dissertations in chemistry in the United States in 1987.

I also received the distinguished dissertation award from the Northeastern Association of Graduate Schools,

which was a consortium of about 60 graduate schools in the Northeast United States. So that was for all fields of physical sciences and engineering from the period from 1983 to 1987.

Q. Could you summarize for the Court your professional experience after your post-doctoral research?

A. Yes. So I have held faculty positions at the University of Alberta, Indiana University, and Kansas State University.

Q. And have you been a visiting professor?

A. Yes. Sorry.

Q. Anywhere?

A. Yes. I've also been a visiting professor at the university of Rennes in France, ten different occasions since 2001, and I was a visiting professor in the chemistry department, University of Bordeaux, in 2006. So in Rennes, it was in the department of physics.

Q. And at a very high level, could you briefly summarize for the Court the focus of your research during that your academic career?

A. Yes. So throughout my academic career, we focused on properties of crystals, including chemical and physical properties of crystals. We've had particular interest in the optics of crystals and diffraction properties. We've studied phase transitions, the mechanism of crystal growth,

the mechanism of phase transitions and other physical transformations, and we've used all sorts of different types of spectroscopy and microscopy studies.

Q. Have you published in peer-reviewed journals and books on the subject of organic chemistry?

A. Yes. I have approximately 45 publications, seven of which have appeared in either science or nature, so this includes two book chapters. Also given presentations at national and international meetings. Virtually, all of these had to do with solid state organic chemistry and the property of crystals. So much of our work lately is focused on phase transitions and solids.

Q. Have you served as appear reviewer for scientific journals?

A. Yes, I have. So I've been a reviewer for Science and Nature, Journal of American Chemical Society, Chemistry Materials, Molecular Crystals and Liquid Crystals, Journal of Pharmaceutical Sciences, and I could go on. There are quite a few.

Q. At Farber Research, have you gained expertise in thermal analysis and other variable temperature methods?

A. Yes. So we've had a DSC in our laboratories since 1995, and temperatures are a variable we use throughout our research. We're interested in phase transitions, so we use variable temperature, X-ray diffraction, nuclear magnetic

resonance, spectroscopy, microscopy, as well as different types of thermal methods.

Q. And the thermal methods you described, what do they have to do with melting points?

A. Well, sometimes we use the thermal methods to measure melting points.

Q. Have you previously been recognized as an expert on solid state chemistry issues for organic pharmaceutical compounds at trial?

A. Yes. I've been recognized twice.

Q. Can you please open your binder to DTX-77?

A. My screen -- yes.

Q. And what is DTX-77?

A. That's my C.V.

Q. And is this a true and accurate copy of your C.V. up to the point you've provided it?

A. Yes, it is.

Q. And is it an accurate summary of your educational and professional achievements at this point?

A. Yes.

MR. ABRAMOWITZ: Your Honor, we would offer DTX-77 into evidence.

MR. LIEF: No objection.

MR. ABRAMOWITZ: Your Honor --

THE COURT: It's admitted.

(DTX-77 Exhibit was admitted into evidence.)

MR. ABRAMOWITZ: Your Honor, we tender Dr. Hollingsworth as an expert in the field of solid state chemistry and the thermal analysis of organic and pharmaceutical compounds.

MR. LIEF: With those topics as described, no objection.

THE COURT: All right. He's admitted as an expert.

BY MR. ABRAMOWITZ:

Q. Dr. Hollingsworth, have you prepared some demonstratives to help with your testimony today?

A. Yes, I have.

MR. ABRAMOWITZ: Could we go to the demonstrative?

BY MR. ABRAMOWITZ:

Q. First, could you explain to the Court what you were asked to do in this case?

A. Yes. So I was asked to evaluate testing on Zydus' magnesium stearate as well as to look into the literature of magnesium stearate and its thermal properties.

Q. Could you provide some background? You talked about magnesium stearate. Could you provide some background as a chemist on the chemical nature of magnesium stearate?

A. Yes. So magnesium stearate is a magnesium salt of

stearic acid. This is a long chain fatty acid that contains 18 carbons.

In the commercial, magnesium stearate is mixed with magnesium palmitate, which is another long chain fatty acid salt that contains 16 carbons. And so both of these mixtures can exist either as hydrated phases, that is contained in water, in particular, dihydrate, trihydrate phases as well as anhydrous forms.

Q. Has the thermal behavior of magnesium stearate been published in the literature?

A. Yes. There's a wealth of publications on the behavior of magnesium stearate.

Q. Can we see the next slide, DDX-6.4. Have you reviewed this literature?

A. Yes, I have. I looked carefully at it, and the literature is consistent in that the authors all agree that magnesium stearate undergoes a dehydration in a solid state with a solid phase transition to an anhydrous form beginning at or below a hundred degrees Centigrade. You can also do this by evacuation of the material at room temperature or other temperatures above that.

And so --

THE COURT: What do you mean by evacuation, Doctor?

THE WITNESS: I mean that you can remove the

water by applying a vacuum to the sample. And so the literature also is consistent in reporting that the anhydrous form melts in a separate endothermic event at or above 105 degrees Centigrade.

So many different analytical techniques have been used to examine this transformation.

Q. Have you reviewed any testing on Zydus' actual samples of magnesium stearate?

A. Yes, I have.

Q. And what types of testing did you review?

A. Well, I reviewed hot stage microscopy provided by defendants. I reviewed DSC provide by both plaintiffs and defendants and TGA from plaintiff.

Q. Have you prepared some demonstrative slides to help the Court understand what is actually taking place in the magnesium stearate samples?

A. I think we need some background. The next slide talks about the classification of different types of solids. Basically, there are three different types of solids. There are crystalline solids, mesophases and amorphous solids.

And crystalline solids exhibit long range orders in three dimensions. That is their distinguishing feature. Mesophase, on the other hand, exhibit long range order extending in one or two dimensions. And amorphous glass have short range order only.

Q. What are the unit cells?

A. So a unit cell is a -- a typical unit cell is shown on the next slide.

This case is fundamental building block of a crystal. It's basically a box of a certain size and shape that contains molecules or atoms in specific arrangements.

And so as you can see on the next slide --

Q. And the slide you're looking at currently, Dr. Hollingsworth, is DDX-6.7?

A. I am sorry. Yes. I'm sorry. I didn't hear your question.

Q. And are you looking at DDX-6.7 currently?

A. That's correct.

Q. And can we go to DDX-6.8.

A. Yes. So the next slide just shows that crystals are built up from unit cells that repeat in all three dimensions. That's what I've shown in this, in this slide.

Q. Do solid state chemists and scientists have some form of shorthand to explain how crystals are arranged?

A. Yes. So the next slide is a graphic showing different, the seven different main symmetry classes for crystals, and this is important in the present case, because there's some confusion over these terms.

And so isotropic crystals -- well, cubic

crystals are isotropic. In cubic crystals, the length of the unit cell are equal. That is all three lengths are equal, and the angle between those unit cells is 90 degrees.

And so cubic crystals are said to be isotropic. Their properties are the same in all directions.

The next class is made of uniaxial materials. These are hexagonal, tetragonal and trigonal. The thing that distinguishes them, they have one axis, that is the vertical axis called the C in these diagrams. Okay. That's a certain length. And then the other two axes, A and B, which are perpendicular to C, that have equal lengths. And so that makes A and B equivalent. And the properties of uniaxial crystals are equivalent in the AB plane. So that's why they're called uniaxial. They're said to be isotropic when viewed along the unique axis, which is the vertical axis in this diagram.

Then there are low symmetry crystals, which are anisotropic in all directions. Those are orthorhombic and monoclinic and triclinic. Here there are no restrictions on the length of the sizes in the cells. Orthorhombic and monoclinic cells have some restrictions on the angle between those spaces.

Q. Looking here at DDX 6.9, were you here yesterday to hear Dr. Pinal testify?

A. Yes. I think Dr. Pinal had a basic misunderstanding of what the literature is meaning when it talks about loss of isotropic in experiments in the literature, and certainly in the videos I have seen we're looking down the unique axis of these crystals, as we see when I talk when that a little bit later. The crystals when they are uniaxial look to be isotropic in that AV plane.

Q. Now, you may have heard Dr. Pinal talk about cross polar as an anisotropic. Have you prepared a demonstrative to show that?

A. Yes, I have.

Q. Can we turn to DDX 6.10. What's going on in DDX 6.10?

A. This next slide is a set of photographs from research. Notice that the background color is purple instead of black. In many cases we use cross polar that will give a black background. Here. We have a compensated plate that gives a purplish color to the diagrams or to photographs. And so in this, in this series of photographs, if the system is purple, then it would appear black between the cross polars. This is a phase transition that takes you from a trigonal high temperature form which is isotropic in the plane of plate face just like the glasses to a low temperature orthorhombic form in which you can have light passing through the crystal and see different interference colors when viewed through this plane. Then so that happens at

around minus 175 or so.

As you warm the crystal up from the low temperature orthorhombic phase to the trigonal phase, it now becomes isotropic in the plane in that magenta and has the same color as the background.

What we're doing is changing the symmetry of this crystal at very lot temperatures, we go from a high symmetry crystal to a low symmetry crystal in a solid-solid phase transition going back to other way, we have essentially recrystallized this sample to give a high symmetry crystal again.

Q. Doctor, does this recrystallization here involve a melt?

A. No.

MR. LIEF: Your Honor, if I might, I do not recall this in his report. I don't believe this is a part of what's been exposed --

THE COURT: When you say this, what is the "this?"

MR. LIEF: This entire discussion, the prior answer and this question as well.

MR. ABRAMOWITZ: Well, respectfully --

THE COURT: You've got to talk to me, not him.

MR. ABRAMOWITZ: Your Honor, in paragraph 42, 61 through 63 of Dr. Hollingsworth's report which I can

provided, Dr. Hollingsworth talks at length about anisotropic, and during Mr. Lief's deposition.

He talked about phase transitions just this way and using cross polars in his laboratory, very low low temperatures to elicit the difference between looking through the plate phase and seeing nothing and looking through the plate phase and seeing colors or antitrophic. This is a demonstrative illustrating his testimony.

MR. LIEF: I didn't hear anything in that answer that in his report there is a discussion of that decanedione/urea ferroelastic phase transition, I didn't hear it. I think this is brand-new.

MR. ABRAMOWITZ: We agree the molecules is a demonstrative.

THE COURT: If you received the demonstratives and had a chance -- let's put it this way. I'm overruling the objection assuming his report contains what I just heard Mr. Abramowitz say. They take this to be an illustrative of the anisotropic and isotropic nature of the material that is heated or goes through a transition. All right?

So you'll have a chance to cross-examine him on it if you'd like.

If you're going to tell me hey, he never talked about the isotropic and anisotropic changes in his report, that's one thing, but if you're saying he never pointed to

urea ferroelastic phase transition and that's what's bothering you, then I'm not worried about that because I take it that this is illustrative of something that's been gone over at length with your witness and which I expect, unless again, Mr. Abramowitz represented to me is covered in this man's report.

MR. LIEF: Again, I don't believe that this whole discussion with trigonal and orthorhombic, these are remarkable I think details that I don't recall from this.

THE COURT: All right. Well, why don't we move forward because unless I'm badly missing my bet, I've just gotten some background information about phase transitions here.

Okay. Go ahead.

BY MR. ABRAMOWITZ:

Q. We've heard Dr. Pinal talk about solvates and hydrates. What are solvates and hydrates?

A. The next slide, the demonstrative shows that. The solvates and hydrates are physical forms that contain solvent on molecules in their three-dimensional structure. So one class of solvates are hydrates. They include water. They're very different types of hydrates and oftentimes they're characterized by the geometry of water. In monohydrate, they have a one-to-one ratio. Dihydrates have two-to-one. Trihydrates have three-to-one. You can have

anhydrates that are crystalline forms that are not solvates.

Q. Dr. Hollingsworth, what's a liquid?

A. The next slide is a demonstrative that tells us about that. So we all know from common experience that liquids flow and they fill up the volumes of their containers, but the important thing here is liquids are isotropic, they have properties of the same and in all direction.

So another further constraint on a definition of liquid is a geometric ordering/correlations disappear after only a few molecules. If you look at the x-ray diffraction pattern of a liquid, we get broad bands with radial symmetry, and this represents the most common distances between molecules as it turns out.

Q. Dr. Hollingsworth, how are solvents and liquids related?

A. Yes. So they're related to phase transition. So the next slide shows an example of phase transitions. So if you heat a solid, you can melt it. That's a phase transition, takes you to a liquid.

You can evaporate a liquid and a phase transition takes it to a gas. A gas can be condensed, that's the reverse of that evaporation phase transition, that gives a liquid and you can freeze crystalize, a liquid, to get a solid.

So on the top of this diagram. I have separated

these in terms of which way the heat flows, so going to the right, you have an endothermic transition when you go from a solid to a liquid or a liquid to a gas that absorbs heat. Going from the left, condensation or freezing, it's heat releasing or exothermic.

Q. Here, Dr. Hollingsworth, are you looking at DDX 6.13?

A. That's correct.

Q. Are there any other types of phase transitions?

A. Yes. So you can have all sorts of different types of phase transition. I have separated these in terms of whether or not they're endothermic or exothermic. We have heard melting or boiling which is endothermic.

We have the last transition which takes you to a molting state, amorphous. You can also have solid-solid phase transitions that are either endothermic or exothermic.

One type of solid-solid phase transition takes you from a crystal to another or crystal to mesophase. That's always going to be endothermic. And desolvation or dehydration which is loss of bound solvent/water that's going to be endothermic.

On the exothermic side, we have freezing including crystallization from a melt, condensation which we just saw, going from amorphous to a crystalline phase is exothermic, hydration and solvation is exothermic. Like I said, solid-solid phase transitions can be either exothermic

or endothermic.

Q. There is some highlighting on DDX 6.41. Why are these highlighted?

A. I have highlighted the ones that are relevant to this case. That's melting, solid-solid phase transitions, including crystals and mesophase and desolvation/dehydration. Those are all endothermic on the right side. Exothermic transitions of relevance can include freezing including crystallization from a melt.

Q. What types of solids melt?

A. So either a crystalline solid or mesophases can melt.

Q. Can you provide the Court with a definition of melting point?

A. I have got a demonstrative for that.

So the Court's definition is widely accepted and the correct one, that's the temperature at which a solid and liquid phase of a compound are at equilibrium.

This diagram is from Maria Kuhnert-Brandstatter's book, Thermal Methods -- now I have forgotten the name of the book, but it's her book on Thermal Microscopy of Pharmaceutical Compounds show a very nice example of an equilibrium melting point.

Here, she's adjusting the temperature of this sample, so first to raise the temperature, so this particular crystallite starts to melt and then she's

reversed the sequence and lower the temperature just a tiny bit to make the crystallite reappear again. So she is --

THE COURT: So I may come back and read this, so I got to make sure we're talking about this in the way that will be reflected on the record, Dr. Hollingsworth.

You're looking at DDX 6.15, and when you say here she is raising the temperature, you pointed in the upper left-hand corner and moved to the upper right-hand corner. Did I get that correct?

THE WITNESS: Yes. Sorry. So you start at a somewhat lower temperature or maybe a particular temperature and at that temperature the crystallites start to melt. You see, you watch it melting up in the upper two frames at a particular temperature, then the temperature is lowered very slightly, maybe only by a few tenths of a degree, and the crystallites starts to regrow, and even larger as it remains at that temperature or possibly a slightly lower temperature. This is a way of homing in to the equilibrium melting point of a solid.

THE COURT: And the recrystallization is represented in the bottom two photographs moving from the left to the right; correct?

THE WITNESS: Going from the upper right you can see the particle is smallest there. I think it probably gets a little bit thicker as you go from the lower left, and

then it certainly is larger in the lower right frame.

THE COURT: Thank you.

Q. And Dr. Hollingsworth, is Professor Kuhnert-Brandstatter a well-known authority on microscopy?

A. She is wildly recognized an authority in the field.

Q. Is her work a well-known treatise that's used as both a teaching and learned text?

A. Yes.

MR. ABRAMOWITZ: Your Honor, we move in figure six from DTX 89.

MR. LIEF: No objection.

THE COURT: Admitted without objection.

BY MR. ABRAMOWITZ:

Q. Have you looked at any articles or text to explain what is met by an equilibrium melting point?

A. There are many, several of which are included as exhibits in my report. So this is a chapter by David Grant in Brittain's book on polymorphism and pharmaceutical, in this chapter he has a diagram called the energy versus temperature diagram. This is a general diagram, it's G1 and G2 could represent the parameters either for two different crystal forms or G1 could represent a solid and G2 could represent a liquid.

And so the point about this is that this gives the definition of a graphical meaning to the definition of a

melting point.

The melting point is defined as the temperature at which these two curves cross, that is the free energy of the solid and the free energy liquid each have a characteristic free energy at different temperatures, so the temperature at which they cross, the free energy difference between solids and liquids is zero, they're equal to each other.

Q. Dr. Hollingsworth, are you looking at Figure 10 from DTX 81 on DDX 6.16?

A. That's correct. The point is that at the melting point the equilibrium melting point as been defined by this Court the difference in free energy is zero.

Q. And Professor Grant who wrote this chapter, was he a well-known solid state expert?

A. Yes, he was a editor of the Journal of Pharmaceutical Science for many years.

Q. And the book the theory of polymorphism, Harry Brittain's book, is that a well-known treatise in the area of solid state pharmaceutics?

A. I think the name is polymorphism, it's a well-known and well-regarded treatise.

MR. ABRAMOWITZ: Your Honor, we move in figure 10 of DTX 81.

MR. LIEF: No objection.

THE COURT: Admitted without objection.

BY MR. ABRAMOWITZ:

Q. Have you prepared any other demonstratives helping to claim how the melting point works in?

A. That last slide is a little busy slide, I have simplified it so we can see what's going on here. Here again we have a free energy versus temperature diagram.

Q. We're looking at DDX 6.17?

A. That's correct. And so this is a free energy versus temperature diagram for a liquid and a solid, so you can see the point where the two curves cross, that's the temperature at which the solid, the free energy and the solid and the liquid are equal to each other. This is how a melting point is defined.

Q. Does this phase diagram have any, on DDX 6.17, have any reference to Dr. Pinal's opinion about the onset melt in the DSC thermograms?

A. In the demonstrative that Dr. Pinal showed yesterday, he showed a position that would correspond, or the onset of which is a position on this graphic corresponds to something to the left of equilibrium point.

There at those temperatures there is a bias in favor of the solid over the liquid. So it's not the thermodynamic of a melting point. It's far from it.

Q. Is there a position on this graph that corresponds to

the equilibrium melting point of the DSC?

A. Well, I think the best position is the one that corresponds to the peak maximum for the endotherm, that's probably the closest you can get to the actual melting point.

Q. Can you describe the phase condition from the crystal from mesophase?

A. The next slide, the graphic that shows that, just as de Genne stated on the first page of the book, that's DTX 78, often times instead of going directly from a crystal to a liquid, you go through a mesophase or a series of mesophases, instead of having three-dimensional long range order, they have one or two dimensional long range order of their lattice, they're still anisotropic. And finally the mesophase can melt to give a liquid which is isotropic.

Q. We're looking at DDX 6.18 which contains some information which contains information from the de Gennes 78. Was Professor De Gennes an important person in the world of mesophases?

A. He won the Nobel Prize in physics for his study of liquid crystals.

Q. And have you prepared any other slides concerning how mesophases work in transitions between crystals and liquids?

A. As I said, on the first page of de Genne's book, he talks about the fact that many materials go from a crystal

through a series of different mesophases to a liquid, so they pass through a series of different phase transitions that take you from one mesophase to another and then finally give a liquid.

Q. Given this background and these slides you presented, Dr. Hollingsworth, can you kind of give the Court an explanation of what and analytical methods were used to study the actual samples of Zydus's mesalamine?

A. So the three methods that were used to study mesalamine samples were hot stage microscopy, differential scanning calorimetry, DSC, and thermogravimetric analysis.

Q. What is hot-stage microscopy?

A. Hot-stage microscopy is a method that utilizes a microscope and hot stage heating elements and temperature controller and it's nowadays always used in conjunction with a video camera and/or a photographic camera to record the event.

Q. How does a hot-stage microscopy experiment typically work.

A. Typically the temperature is ramped up at a constant rate or down at a constant rate and the changes in the sample are viewed through the microscope and with these devices.

Q. Have you prepared a demonstrative to show the Court what typically happens under the microscope when a

crystalline compound melts?

A. The next slide shows a very nice example from Walter McCrone's book. It's called Fusion Methods in Chemical Microscopy. It's DDX 87. Here he shows melting of highly pure azobenzene. In this slide the temperature is up in the upper left, 68 degrees, upper right, 68.2, lower left 68.4 and lower right 68.5. In this diagram I have highlighted certain regions so you can focus on those. Those are in the blue boxes. You can see that this lower left crystallite starts to deform a little bit around 68.2, but then it doesn't disappear until you go from 68.4 degrees to 68.5 degrees. And other particles show slight changes in shape during this temperature range.

I think according to the definition of a melting point the melting point of this particular sample is somewhere between 68.4 and 68.5 degrees.

Q. And Dr. Hollingsworth, who is Professor McCrone?

A. So he was one of the most widely recognized experts in thermal microscopy.

Q. Is his book an authoritative text on the method of thermoscopy?

A. Yes, it is.

MR. ABRAMOWITZ: Your Honor, we move in figure 22 from DTX 87, the McCrone book into evidence.

MR. LIEF: No objection.

THE COURT: Admitted without objection.

BY MR. ABRAMOWITZ:

Q. Dr. Hollingsworth, have you prepared some demonstratives showing the hot-stage microscopy experiments conducted on Zydus samples?

A. Yes, I have. So there are actually two sets here. The first is actually a video that Dr. Sacchetti and his colleagues performed on one sample. You can actually see that the temperature is already going up here. And we'll get to the second one in a second which is just an animation based on a set of photographic stills.

But the point is that as the temperature is raised from 70 through 90 degrees, there are no apparent changes in the crystallites that you observed in the sample. And so the temperature continues to rise and again there are no apparent changes. We can keep going up, there was a refocus there.

Until finally you can start to see some changes appearing I think right around 130 or so, and certainly above 140, you can see that there is a very clear melting process going on.

THE COURT: You may have said it, but I didn't hear it. DDX 6.24 is what we have been talking about; right?

THE WITNESS: Yes.

Q. And the video you were referring to, was that DTX 105?
A. That's correct.
Q. Could we move on to DDX 6.25 with DTX 104. What are you showing in DTX 104 here?
A. This is an animation made from a sequence of photographic stills and here the temperature is going up. There we passed 90 degrees without any apparent changes in the sample as you can see. If the temperature keeps going up, you'll finally see changes at much higher temperature. So nothing at a hundred, there is a refocus there, 120, finally you can see things happening close to 130 degrees. And you can see visible melting at higher temperature.
Q. Dr. Hollingsworth, have you reviewed any additional evidence in the literature that relates to the hot-stage microscopy results seen on Zydus' mesalamine samples?
A. I think the nicest example from the literature is this series of photo micrographs from the paper of Miller and York that is DTX 82. Here in this upper left frame we can see that it's taken at 88 degrees, the middle one in the upper part is 96, and then 101 in the upper right, 121 the lower left, 126 in the center one in the bottom, and 130 in the bottom right.

Let's focus for just a minute on the large crystallite that they have identified in the very first frame. So one thing you see is that it looks like a nice

single crystal that's overlapped with some other crystals. You can also so it's very thin plate and we're looking right down through the plate face of this crystal.

And so that's important because the molecules, the long chain molecules are actually lying side-by-side each other in that plane.

As you warm the crystal, you can -- from 88 to 96 degrees, there is really very little or no change in the shape of the crystal. You can start to see some striation and the authors note that and these become more apparent at 101 degrees. Finally at 121 degrees you can see some deformation in the edges of the crystal. At 126 you can start to see melting and at 130 you can also see melting.

But the other thing that the authors note is that at 96 degrees, the crystal looks anisotropic, this is an important point to this case. The question is what did they mean by that. They're looking right down through the plate face of this crystal. And when the crystal undergoes a solid-solid dehydration, it goes to a higher symmetry form, or what appears to be a higher symmetry form just like those hexagonal crystals or the hexagonal crystals that I showed you or trigonal crystals that I showed you earlier in that demonstrative.

From the point of view of a scientist, this

crystal looks anisotropic in that plane, that's what they're observing.

Your Honor, your question was right on the money, the question was whether or not a loss of anisotropy has anything to do with what the scientists are seeing or overall whether it becomes isotrophic. Overall in the literature, it's consistent that these crystals lose their anisotropy. If you lie down flat and when you look at them with a microscope, you're looking through the plate face. As you'll see, this process takes you to a mesophase that has higher symmetry than the anhydrate -- I'm sorry, than a hydrated phase that was its precursor.

Q. Dr. Hollingsworth, you have been looking at figure five, DTX 82, PTX 504 on DTX 6.27?

A. That's correct.

MR. ABRAMOWITZ: Your Honor, I think figure five is already in evidence, PTX 504, but we would renew offering figure five of PTX 504 into evidence.

THE COURT: If it's in, it's in.

BY MR. ABRAMOWITZ:

Q. Dr. Hollingsworth, what's DSC or differential scanning calorimetry?

A. This is an analytical technique that uses the thermal characteristics of samples to study phase transitions and look to distinguish between the different materials.

Q. And how does DSC work?

A. DSC there are basically two wells, one contains a sample, the other one contains a reference. And in the experiment you heat the sample and reference and supply enough power or energy, thermal energy to the sample and reference to keep them exactly the same temperature during heating or cooling.

Q. What type of data does DSC generate?

A. DSC generates what's called a thermogram. This is a plot of heat flow as a function of temperature, in this particular diagram, endothermic transitions and exothermic transitions point downward.

THE COURT: That's a flip of what we have been seeing on the DSC diagrams that have been created by the experiments we have seen so far; is that right?

THE WITNESS: That's correct.

THE COURT: Can I ask you, why would you have a -- you would have a sample you said and a reference. What would the reference be? What's the point of having some other material?

THE WITNESS: So we go back a slide. It turns out the reference is just the sample pans themselves, they have a certain heat capacity of their own. And these sample pans are made to variate exactly to standard, so this allows you to compare the reference and the sample to the

difference between those wells, but the heat characteristics of the sample itself.

THE COURT: So the reference doesn't contain material in the container.

What's the heat doing to the container, so that you can sort of separate that out from what's happening to the sample?

THE WITNESS: So in both sides you have the container. And the containers are meant to match each other in size and shape and volume and heat capacity. So the difference between the reference which has the container and the sample that has the container containing the sample is the sample. So you try to match the two wells as close as possible so you can actually look at what's happening to the sample.

THE COURT: At the sample by subtracting what's happening to the sample?

THE WITNESS: You look at the differential heat flow between the sample and the reference. That's why it's called differential scanning calorimetry.

THE COURT: Thank you.

BY MR. ABRAMOWITZ:

Q. Can we go back to DDX 6.30?

A. This actually shows representative transitions, an endotherm, a desolvation endotherm for melting and an

endotherm for a solid-solid phase transition, which could have been either endothermic or exothermic. Recrystallization is always exothermic.

Q. Do you have some exemplary traces of real world compounds that you can explain to the Court?

A. This slide is an article by Giron, DTX 98. This is a review on thermal properties of pharmaceutical compounds. This first one, figure 12, is an exemplary trace of dehydration followed by melting for two separate samples so substance A and B here, each of those shows an endotherm from dehydration followed by a melt. One of higher temperature and the other at low temperature. So Giron classifies these sort of endotherms as indicative of what's called type one process, in which is the dehydration occurs in a solid-solid phase transition without melting. So that's the first one.

Q. And Dr. Hollingsworth, before I move on, we're looking at figure 12 from DTX 98, PTX 496, the Giron reference. If you see there are two sharper melting endotherms and the dehydration. I know you heard Dr. Pinal discuss that to some extent, what is the significance of that?

A. Well, those endotherms are actually for a different material, so the dehydration process occurs for the hydrated material, that's a completely different material than what we have at higher temperatures. So the melting here is the

melting of the anhydrate, not of the hydrate.

Q. Is there a special meaning to the sharpness of these two peaks in the meltings?

A. I think the sharpness depends on lots of things, especially the chemical purity and the mechanism by which the sample melts. It doesn't necessarily represent anything about a crystallographic purity as Dr. Pinal was stating.

It really has more to do with the mechanism of melting because there are lots of different cooperative interactions going on during this process, and the chemical purity of the sample.

Q. And in figure 12, the endotherms we're discussing are the features labeled dehydration and melting endotherm; is that right?

A. That's correct.

Q. Do you have some further demonstratives concerning the dehydration process and DSC traces?

A. So figure 13 is another figure from Giron's article. So Giron calls this, the next one a type two dehydration process. You can see very clearly that dehydration here occurs with melt. How do you tell that? Well, there is right after the dehydration and melting endotherm, there is a recrystallization exotherm, so you can tell that sample melted when it dehydrated, then it recrystallized in an exothermic transition to give a melting endotherm for the

anhydrous form. In this particular plot you also see a TG trace that shows loss of mass that corresponds to the dehydration event.

Q. And just so the record is clear, the endotherms you're discussing, figure 13 of DTX 98, PTX 496, Giron, the features labeled fusion and loss of water?

A. Yes.

Q. Which one is the exotherm?

A. Yes, so there is a point of peak labeled liquid with an arrow to anhydrous form, that's the recrystallization exotherm in this diagram.

Q. You just pointed to a TGA. What is a thermographic analysis of TGA?

A. That's in the next slide. This is an analytical -- I guess it's not.

Q. Could we go forward to DDX 6.34 real fast. 6.35. Next slide. One more. There we go. What is TGA?

A. So TGA is just another analytical method that's used to measure mass loss, a sample as a loss of function of temperature, basically a heating element, a microbalance. A sample is heated at a constant rate. This is used to compliment DSC information, used to characterize desolvation and decomposition transition in solid.

Q. Can we go took back to DDX --

THE COURT: Hold on just a moment. In what

sense is it used to compliment DSC?

THE WITNESS: It can help you understand what the particular features of the DSC mean, so in particular if you have a dehydration or a desolvation process, the temperature of the TGA loss matches that of the DSC endotherm that we observed, then those two are correlated by this TGA measurement.

THE COURT: Does one tell you anything about -- does the TGA tell you anything about whether what's happening with an endotherm is a dehydration or a melt?

THE WITNESS: It gives you information about the dehydration process and not about a melting, possible melting, a melting process and recrystallization.

THE COURT: But TGA in terms of whether something is in a dehydration form?

THE WITNESS: That's correct. And sometimes from the features of the TGA we can interpret what we're seeing in the DSC, but in general it's used to document whether or not you have a mass loss which corresponds to the solvation or dehydration.

THE COURT: And does a hydrated form of a chemical compound have to go through a dehydration process before it can melt as a general matter or can the hydrated form go directly to a melt?

THE WITNESS: Well, this depends on what kind of

sample you have, what the crystal structure is. We'll get to that.

THE COURT: It depends on a lot of stuff.

THE WITNESS: That is correct.

BY MR. GAERTNER:

Q. If we go back to DDX-6.33. Could you explain what's going on in the DSC that Dr. Hanton conducted?

A. Yes. So this is Dr. Hanton's DSC of magnesium stearate and he was heating it at a rate of ten degrees per minute. The point is he observed endotherms for dehydration and something that appears to be a melting endotherm. The point about this then, also Sacchetti's results, there's absolutely no evidence for a recrystallization exotherm in this DSC plot.

So the next slide actually shows you what happens with Dr. Sacchetti's DSC. Here he slowed down the heating rate to five degrees per minute. That improves your chances of seeing events that are overlapped, but still he saw no evidence whatsoever for a recrystallization exotherm. The only features that you see in the DSC trace are endotherms for dehydration and for melting.

Q. Doctor, did you look at any DSCs in the academic or scientific literature that helped you to understand the DSC's that were performed by Dr. Hanton and Dr. Sacchetti?

A. Yes, I did. One of them is shown on the next slide.

This one is from a paper by Miller and York. Earlier we saw crystal microscopy of the same samples.

THE COURT: The next slide. We're looking at DDX-6.35. Right?

THE WITNESS: That's correct.

THE COURT: Go ahead.

THE WITNESS: This is from DDX-82. This is from a paper by Miller and York.

Notice that they're heating at two degrees per minute and so on the top, you have magnesium stearate, two different samples, and the bottom you have magnesium palmitate. Powder A in the upper left is the trihydrate. You see an extra endotherm for dehydration in that particular material and powder B on the upper right is the dihydrate. So that actually shows a single endotherm for dehydration and then a melting endotherm.

The same goes for palmitate. You can see endotherms only. None of these DSC traces have any recrystallization exotherms that are evident.

Q. Looking here, Dr. Hollingsworth, at Figure 2 of DTX-82, PTX-504, is there any significance to the heating rate that was used?

A. Yes. Once again, if you slow down the heating rate, you increase your chances of distinguishing overlapping events in the DSC, such as recrystallization exotherm that

overlaps with the dehydration endotherm.

Q. And what heating rate did Miller and York use in DTX-504?

A. They used a heating rate of two degrees per minute. Dr. Hanton used ten. Dr. Sacchetti used five.

Q. Now, if we could go to DDX-6.37, we see Dr. Hanton's TGA. Could you explain what's going on here?

A. So here we have the TGA for Zydus' magnesium stearate and basically what you see is a mass loss. I think losing about 3.6 or so percentage of its mass. This is because of the dehydration. So the documents, the temperatures over which the dehydration occurs, and that matches pretty closely to the large endotherm that you see in the DSC at lower temperature.

THE COURT: And can a TGA curve like that be attributed to anything other than dehydration, the loss of hydrate?

THE WITNESS: Well, this is what you are measuring with the TGA, so the TGA only tells you about what is happening.

THE COURT: Right. My question is: This shows you, if I'm correct, this shows you a loss of mass?

THE WITNESS: That's correct.

THE COURT: Okay. And my question is: Can the loss of mass be attributed to anything other than the loss

of a hydrate?

THE WITNESS: Yes. Sometimes if you have a decomposition of the molecule, if the carboxylate were to lose carbon dioxide, for example, you might lose some, but chemically, that does not make sense in this particular case. There's certainly no evidence that this is anything except water leaving the crystal.

THE COURT: Thank you.

BY MR. ABRAMOWITZ:

Q. And, Dr. Hollingsworth, were you talking here on DDX-6.37 about PTX-552?

A. That's correct.

Q. Did you see any evidence in the literature that discusses TGAs of magnesium stearate samples similar to that seen in Zydus' sample?

A. Yes. So many of the papers show TGA traces including the one by Miller and work we've seen before, DTX-82. So Figure 2 of Miller and York shows dehydration of magnesium stearate and magnesium palmitate.

As I said, the diagram on the upper left again is for the trihydrate. Powder B on the upper right is for the dihydrate. And you can see a single -- I'm sorry, a mass loss right around 100 degrees or so in that, in that TGA at any rate.

Q. And, Dr. Hollingsworth, you're using your laser

pointer to point out a Figure 4. Is that Figure 4 from PTX-504 of the Miller article?

A. That's correct.

MR. ABRAMOWITZ: Your Honor, we move in Figure 4 of the Miller article into evidence.

MR. HAUG: No objection.

THE COURT: Admitted without objection.

(PTX-504 was admitted into evidence.)

BY MR. ABRAMOWITZ:

Q. To sum up, Dr. Hollingsworth, are these testing results that Zydus has made on samples consistent with what you have seen in the literature regarding magnesium stearate?

A. Yes. They are completely consistent with numerous papers on this topic.

Q. What's shown on this demonstrative?

A. This is just a summary of the different articles that I reviewed from the literature. It tells you what kinds of magnesium stearate the authors were looking at and at least some of the analytical tests that were used to study these, these materials.

Q. And starting with the Miller and York articles, DTX-504, what type of magnesium stearate did they study?

A. They were studying purified magnesium stearate.

Q. And what kind of analytical tests were they using?

A. So they used, among other things, DSC, TGA, hot stage microscopy and powder X-ray diffraction.

THE COURT: What does the word "purified" mean in this context?

THE WITNESS: So the commercial grade magnesium stearate contains magnesium palmitate, so instead they actually purchased magnesium, pure magnesium stearate, and then -- I'm sorry. Purchased stearic acid and then converted that into magnesium stearate.

I'm not sure exactly what purification techniques they used, but it was primarily just simply magnesium stearate instead of magnesium stearate mixed with magnesium palmitate.

THE COURT: Thank you.

MR. ABRAMOWITZ: Could we go to PTX-504, internal page 62. And if we could look at -- let's look at the last paragraph.

First, let's look at the second full paragraph, the one starting, the first two endotherms.

BY MR. ABRAMOWITZ:

Q. Is there something in this paragraph that you found important in rendering your opinion, Dr. Hollingsworth?

A. Yes. The first sentence says that the first two endotherms of samples A and C, and the first of B and D are due the loss of bound moisture.

So A and C are magnesium stearate and B and D are magnesium palmitate. They say evidence for this is the absence of these endotherms and dried samples and the weight losses observed, using TGA for untried samples at temperatures corresponding to these endotherms, Figure 4.

Q. And if we go down to the bottom of 62 and the text that continues on page 64, in the last paragraph, was there something reported by Miller and York that you found particularly interesting here?

A. Yes. So they, they looked carefully at this by doing not only DSC and TGA, but also hot stage microscopy. Those are actually the images we looked earlier.

It says it was possible by hot stage microscopy for the effects moisture loss on polymer and particle morphology and refractive behavior. They say this appeared to be more pronounced for regular plate like samples B and D. They say the loss of moisture in these cases was accompanied by the appearance of diagonal striations on the particles, shown occurring for magnesium stearate B at 96 degrees, Figure 5. The particles also lose anisotropic property at this temperature.

And then they go on to say the smaller irregular particles of powders A and C did not show anisotropic behavior. Only slight particle changes are visible over the two temperature ranges where these powders lose

moisture.

Q. And if we go onto the first full paragraph on page 64, was there anything there that you reviewed that help contribute to your understanding of magnesium stearate?

A. Yes. So they distinguished those first comments on the dehydration event from the remaining event. They say, the remaining events, not due to the loss of bound moisture from the powders, are associated with melting.

Q. If we go back to DDX-6.39, you also mentioned the Rajala and Laine articles, PTX-498. What kind of magnesium stearate did Rajala and Laine study?

A. They studied both commercial magnesium stearate which contains magnesium palmitate and also purified magnesium stearate.

Q. And what types of techniques did they use to study these magnesium stearate samples?

A. Again, they used DSC, TGA, hot stage microscopy and powder X-ray diffraction.

Q. If we were to look at PTX-498, can you bring up Figure 1.

What is Figure 1, Dr. Hollingsworth?

A. So Figure 1 shows the powder X-ray diffractograms for the commercial magnesium stearate Batch A and Batch B.

Q. And do these X-ray diffractograms show that the powders were solid?

A. Yes. They have clear diffractions that are characteristic of solid. We'll talk about the details later.

Q. And so if we go to Figures 3 and 4. Dr. Hollingsworth, what does Figure 3 of Rajala and Laine, PTX-498, show?

A. These are DSC profiles of two commercial grade magnesium stearates and one pure magnesium stearate.

Q. And let's look at Figure 4. What does Figure 4 show?

A. Yes. So Figure 4 shows DSC profiles of the dihydrate of magnesium stearate and the anhydrate of magnesium stearate.

Q. All right.

A. This is pure grade magnesium stearate.

Q. Why don't we move on to Figures 5 through 7. If we could overlay them just quickly. What did you learn from Figures 5 through 7?

A. So this is just to show that Rajala and Laine actually did TGA on their samples and so they observed a mass loss right around the temperatures where they observed endotherms in their DSCs at lower temperatures.

Q. And, finally, why don't we look at Figures 8 and 9.

Is there something in Figure 8 that particularly peaked your interest?

A. Say it again.

Q. Is there something in Figure 8 and Rajala and Laine, PTX-498, that in particular peaked your interest?

A. Yes. So what we'll do a little bit later is explore this band right around 21 degrees, and so as we see from Braconni's words, that band is indicative of so called rotator phase or mesophase.

There are also other peaks, depending on the hydration state, that appear that show that these samples can have three-dimensional crystal order as it turns out.

Q. Okay. Can we look at Figure 9. And what does Figure 9 show?

A. Yes. So this is, again, magnesium stearate, Batch B, that's under -- been held under different conditions. So the one in the front is after drying and the one further back in the diagram has to do with magnesium stearate held under different humidity conditions.

Q. And just to keep the record clear, which batches in PTX-498 were the commercial batches?

A. Batches A and B were commercial batches. Batch C was the purified magnesium stearate.

Q. And can we go to page 181 of PTX-498. Could you highlight the second full paragraph?

Were there any helpful comments by Rajala and

Laine that you reviewed in forming your opinion? And on page 181?

A. Yes. So, in particular, they are talking first about Batch A of magnesium stearate, or about in the middle of the paragraph, they were -- let me just find it.

They say, previous workers have assigned the low temperature endotherms to the loss of bound water from the crystals and the high temperature endotherm to a melting phenomenon. References 10, 11, 16. Hence, the first two endotherms of the Sample A and the first two endotherms of sample B and C were due to the loss of bound moisture. The evidence of this was the mass losses observed using TG for undried samples at temperatures corresponding to these endotherms. That's Figure 5. They say, the remaining thermal events are associated with melting.

Q. The last paragraph of page 183 that goes over to page 184.

Dr. Hollingsworth, is there any information in this paragraph from 183 to 184 that informed your view of what happened to magnesium stearate during thermal heating?

A. Yes. So Rajala and Laine's observations parallel those of Miller and York. They say, the effective moisture loss on powder particle morphology and refractive behavior was studied by hot stage microscopy. This appeared to be

most pronounced for regular plates such as sample C. The loss of moisture from the sample was accompanied by the appearance of diagonal striations in the particles at about 95 degrees Centigrade.

The loss of moisture resulted also in darkening of the appearance of the crystals when used under crossed polarized light, indicating a loss of their anisotropic property, as has been described previously. That's Reference 10.

And they say the plate-shaped appearance of the original dihydrate was retained until melting at about 125 degrees. They say, the smaller, irregular particles of powders A and B did not show anisotropic behavior. And that only slight particle changes were visible over the temperature range where those powders lost moisture.

Q. Now, Dr. Hollingsworth, the Rajala and Laine articles appeared in the Journal "Thermochimica Acta." Is that a well-known and appreciated journal?

A. Yes.

Q. And what type of reactions did "Thermochimica Acta" normally discuss?

A. They discuss thermal events often in solids, but in other faces as well.

MR. ABRAMOWITZ: Your Honor, we offer into evidence Figures 1, 3, 4, 5, 6, 7, 8 and 9 of PTX-498, the

Rajala article.

MR. HAUG: No objection.

THE COURT: Admitted without objection.

(Figures 1, 3, 4, 5, 6, 7, 8 and 9 of PTX-498 were admitted into evidence.)

BY MR. ABRAMOWITZ:

Q. If we can go back to DDX-6.39. Let's talk about for a moment about the Ertel and Carstensen article.

Dr. Pinal talked about the article yesterday; is that right?

A. That's right.

Q. And what does Ertel and Carstensen say?

A. They were looking at purified magnesium stearate.

Q. And what type of analytical test did they use?

A. They used the DSC, TGA and hot stage microscopy among other technique.

MR. ABRAMOWITZ: Let's pull up Figure 5 of DTX-498. I'm sorry. 499. Excuse me. PTX-499.

BY MR. ABRAMOWITZ:

Q. What does Figure 5 of PTX-499 show?

A. This is the TGA for one of their samples. They name it as Form A.

Q. And could you also pull up Figure 7 of Ertel and Carstensen. And what does Figure 7 show?

A. Figure 7 is the DSC for the same sample, Form A,

which is the magnesium stearate dihydrate, and you can see that the heating rate is two degrees per minute, and still they saw no evidence for a recrystallization exotherm in this DSC trace.

Q. And is there a -- and go to page 176 in the right column.

Is there some information here in this right column that you found particularly helpful in understanding the mesophase aspect of the dehydration?

A. Yes. So in addition to DSC and TGA, Ertel and Carstensen also used powder X-ray diffraction, and they say of particular interest is the region near two theta equals 21 degrees.

They say the diffractogram of the dihydrate exhibited several distinct peaks in this region, while in the case of the anhydrate, these peaks were replaced by a single broad peak. This type of peak is known as a halo, and is indicative of a structure in which the magnesium atoms of magnesium stearate are arranged in irregularly spaced parallel plains. The three-dimensional structure of the crystal lattice has been disrupted. And they cite Vold, 1949.

MR. ABRAMOWITZ: Your Honor, we offer into evidence Figures 5 and 7 of PTX-499, the Ertel article.

MR. HAUG: No objection.

THE COURT: Admitted without objection.

(Figures 5 and 7 of PTX-499 were admitted into evidence.)

MR. ABRAMOWITZ: If we go back to the summary slide.

BY MR. ABRAMOWITZ:

Q. Did you also review the Sharpe, et al article, PTX-497?

A. Yes, I did.

Q. What were they studying?

A. They were studying purified magnesium stearate.

Q. And what type of analytical test did they do?

A. So among other things, they used DSC, TGA and powder X-ray diffraction.

MR. ABRAMOWITZ: Can you pull up the title page from PTX-497? Thank you.

BY MR. ABRAMOWITZ:

Q. Now, you may have heard Dr. Pinal speak about the Sharpe article yesterday. Are any of the authors of the article noticed in the solid state pharmaceutical field?

A. I would say Harry Brittain is the most well-known author. He authored this article. Ann Newman is also a well-known pharmaceutical scientist in her own right.

Q. If we could look at Figures 1 and 2 quickly.

What does Figure 1 of Sharpe PTX-497 show?

A. So this shows both TGA and DSC traces for the anhydrate phase of magnesium stearate.

Q. And what does Figure 2 show?

A. Figure 2 shows the TGA and DSC traces for the dihydrate phase of magnesium stearate.

Q. And are Figures 1 and 2 of Sharpe consistent with the results that were seen by Miller and York and Rajala?

A. Yes, they are. They are all consistent.

Q. Why don't we look at Figure 7.

So Figure 7 looks somewhat different from the figures we looked at. Can you explain to the Court what Figure 7 of Sharpe 497 is?

A. Yes. So in this figure, Sharpe and co-workers are giving a schematic view of the structure of magnesium stearate dihydrate and trihydrate, and what they show here is that they only show parts of the long chain stearate chain, but the most important thing is that the water molecules in the dihydrate and trihydrate are located in the interlayer spacing between these long chains. So the implication is that this is actually a layered hydrate.

MR. ABRAMOWITZ: Put up Figure 8.

BY MR. ABRAMOWITZ:

Q. Is there something notable about Figure 8, the XRPD work that Sharpe, et al did?

A. Yes. So Sharpe and co-workers as well as others show that there are differences in the X-ray diffraction pattern between the trihydrate, the dihydrate and the anhydrate.

In the anhydrate, and we'll discuss this in just a few minutes, there's this band which Bracconi characterizes as a so-called rotator band, which is from a mesophase. There are also sharp peaks at lower angles that correspond to the very long spacing of the long chain molecule.

Q. Okay. If we look at page 80 of Sharpe, DTX-497.8 in the right column, the last paragraph before the heading, does this paragraph provide you some information about the actual structure in magnesium stearate hydrates?

A. The first part of this states that the magnitude of the long crystal spacing associated with the anhydrate and dihydrated phases were comparable, 48.7 and 48.1 angstroms, respectively, but the long crystal spacing obtained for the trihydrate face was slightly larger. These data would permit the deduction that dehydration of the dihydrate phase to the anhydrate phase is accompanied by a slight expansion of the lattice, and that the rehydration of the anhydrate phase to the trihydrate phase is accompanied by a further expansion.

This trend supports the conclusions of Müller, et al, who deduced that the water contained in magnesium

stearate was not present between the intermolecular planes, and was not an integral part of the crystal.

Q. I want to make sure. Was not present or was present?

A. I'm sorry. Was present between the intermolecular planes and was not an integral part of the crystal lattice. Sorry about that.

THE COURT: Okay. Do you want to explain to me what the word "lattice" means in this context?

THE WITNESS: Yes. So the word "lattice" is sometimes misused to mean crystal structure, so a three-dimension medical structure, a lattice is just a series of points, and a structure is a set of atomic positions that are placed on those different points that go in three dimensions.

And so it's actually a mathematical construct, but it's often used interchangeably with crystal structure, which actually means the structure of the solid itself.

THE COURT: All right.

THE WITNESS: Basically, they are saying that the water molecules are not an integral part of the structure, I think here. That is, they're contained in the plains between these long chain molecules.

THE COURT: All right.

THE WITNESS: And that when you dehydrate the sample, you only see minimal change in the overall

structure. So that's what they are talking about here with the long spacing being 48.7 and 48.1 angstroms, respectively, for the anhydrate and dihydrate phases.

BY MR. ABRAMOWITZ:

Q. And later on, shortly, have you prepared some demonstratives that will help explain what Sharpe, et al, are talking about?

A. Yes.

MR. ABRAMOWITZ: Your Honor, we offer into evidence Figures 1, 2, 7 and 8 of Sharpe, PTX-497.

MR. LIEF: No objection.

THE COURT: Thank you, Mr. Lief. They're admitted without objection.

(Figures 1, 2, 7 and 8 of PTX-497 were admitted into evidence.)

BY MR. ABRAMOWITZ:

Q. Finally, can we talk about Bracconi? What is Bracconi citing?

A. Bracconi studied a commercial grade magnesium stearate.

Q. And Bracconi used sort of a different type of test than everything else that we've talked about today?

A. Yes.

Q. What did Bracconi used?

A. He used variable temperature powder X-ray diffraction.

Q. If we go to Figure 4 of PTX-493 of Bracconi. What's going on in Figure 4, Dr. Hollingsworth?

A. Yes. So this is sort of a busy slide, but it's, these are diffractograms, powder X-ray diffractograms as the function of treatment of the sample at different temperatures. And so the very top trace shows the powder X-ray diffractogram of as received sample. This was the sample labeled BG by the author. So fairly highly crystalline material.

And so the important thing is that you can see these peaks 5A, 5B, and 5C that change their shape and intensity as the sample is warm. So the second trace shows what happens after the sample is held at 50 degrees Centigrade. The third one after it was held at 55 degrees Centigrade. And the last one, the fourth one, shows what happens after the sample is held at 69 degrees Centigrade.

So peak 5A represents the trihydrate, so they can tell that from the D spacing or diffractogram spacing. Peak 5B is the dihydrate.

And peak 5C is the anhydrate. And so what they show is that as you hold the sample at different temperatures, 50, 55, 69 degrees, the trihydrate disappears. That's starting to happen at 50 degrees. It's replaced by dihydrate and anhydrate.

And then by the time you get to 55 degrees,

there's very little dihydrate left. That's the peak 5B. And it's almost all anhydrate. By the time you get to 69 degrees, it's virtually all anhydrate.

And so this, in this diagram, they also show on the lower right the so-called rotator band, which we'll be focusing on in just a few minutes. That's characteristic of this mesophase that's generated by evacuating or removing water from the sample.

MR. ABRAMOWITZ: If you could look at figures 5 and 6 on internal page 117.

BY MR. ABRAMOWITZ:

Q. Dr. Hollingsworth, have you prepared some demonstratives that you are going to talk about later that deal with figures 5 and 6 in some great detail that helps inform about the dehydration process of magnesium stearate?

A. Yes, I have, so we'll get to those in due course.

Q. Okay. And why don't we look just real fast at Figure 7 for a couple minutes.

What does Figure 7 have to do with the melting of magnesium stearate?

A. So Figure 7, a series of powder X-ray diffractograms for samples held at four different temperatures, 105, 113, 123, and I think that's 128 degrees Centigrade.

You can see in the lower two traces, especially the lowest one at 1005 degrees, that there's this very

strong brand, 3.34 angstroms. I will explain what the 3.34 means in a little bit. That's characteristic of the so-called rotator phase or mesophase that's generated by dehydration. There's a little bit of that left at 113 degrees and then by the time you get to 123 and 128 degrees, the rotator band for the mesophase is essentially gone.

Q. So Dr. Hollingsworth, having reviewed these five articles, have you formulated any of your own opinions about how dehydration is achieved with magnesium stearate?

A. Yes, I have.

Q. Have you prepared some demonstratives to explain that?

A. So, the literature is very consistent in its description of what's going on, so basically we know from different crystal graphic data that the water molecules are held in the interlayer spaces between the long chain molecules of magnesium stearate, so it's a layer hydrate. So upon heating, the water molecules exit the crystal from these interlayer spaces. This results in a small change in the spacing between the planes without disturbing the solid state structure. The molecules are staying in place as the water molecules leave.

So, hot stage microscopy, there is an absence of a change in crystal shape and that really unambiguously demonstrates this is a solid-solid phase transformation

without melt. This is actually not as Dr. Pinal described as a violent event, it's actually a very gradual event that occurs from this layered hydrate with the water molecules coming out of the crystal.

MR. ABRAMOWITZ: And before I forget, we offer into evidence the figures four, five, six and seven Bracconi that we just looked at PTX 493.

MR. LIEF: No objection.

THE COURT: Admitted without objection.

BY MR. ABRAMOWITZ:

Q. Can you explain exactly how dehydration works in crystals?

A. Yes. So we got a slide for that. This is from a chapter by Harry Brittain in his book on polymorphism of compounds, here is a summary of the different sorts of dehydration mechanisms that accepted and well-known in the literature.

His classification scheme comes from a paper by Galwey. We'll see more of that in just a second. From DTX 93 we see that there are several different mechanisms for dehydration that have been considered and reported in the literature. The first four of these, I won't enumerate them all, are solid-solid phase transitions without any melting of the material going on. The last two involve some melting or comprehensive melting of the solid.

Q. And is the Brittain book DTX 93? Dr. Hollingsworth is the Brittain chapter DTX 93?

A. Yes, it is.

Q. Do you have any further demonstratives?

A. Hang on just one more second, I just want to say that I have highlighted the third one of these, this is a solid-solid phase transition because this is the one that's relevant in this particular case, this has to do with the interface advance and nucleation and growth or contracting envelope that occurs in the solid-solid phase transition, that's the mechanism that appears to be going on --

THE COURT: Hold on, you got to let him finish all the way before you start talking.

THE WITNESS: I said that's the mechanism that appears to be going on in this particular case, with the magnesium stearate.

Q. Sorry. And how do you know what's going on? Do you have a demonstrative that helps explain that?

A. Yes. Let's talk a little more detail about these mechanisms. This is a paper by Galwey, DTX 92. So Galwey classified these dehydration mechanisms according to their water evolution type or WET mechanism. The first four of these on this slide are solid phase dehydration processes. The one of interest is number -- is step C, this is the so-called Wet 3 process.

What we saw in the Miller and York paper was that the crystal retained its shape during the dehydration process from 88 to 96 degrees, there was no noticeable change in the shape of the crystal. That's what Galwey means when he says topotactic reaction. That means there is a correspondence between the initial crystal phase and the orientation of the final phase that's generated in the dehydration.

So the other thing that was noticed by Miller and York was there is some cracking. This has to do with strain that develops in the sample because the lattice spaces in the sample after dehydration do not quite match the lattice spaces beforehand.

There are other more perfect examples up above where you have either no crystal spacing change or something that's topotactic with no cracking. What we're observing in this particular case is a case of cracking just because the unit itself, the parameters have changed enough so you can see some strain in the crystal. This is a solid state mechanism.

Q. Did Galwey explain what happens when a dehydration involves a melt?

A. So the next slide shows that, so the very last so-called WET mechanisms, five and six involve melting. Here they say melting may be accompanied by reactions other

than dehydration. But there you make a melted product during the dehydration. That's not what's going on here though.

MR. ABRAMOWITZ: Your Honor, we offer into evidence figure one of DTX 92, the Galwey article.

MR. LIEF: No objection.

THE COURT: Admitted without objection.

BY MR. ABRAMOWITZ:

Q. Do you have any examples of crystalline solids that dehydrate while melting?

A. Sure, I do. So one nice example is Lidocaine hydrochloride monohydrate. So what you can see here are these red circles, those correspond to water molecules in the crystal structure so the thing about these water molecules is not only are they held tightly by hydrogen bonding and electrostatic forces, they're buried within the crystal, there is no easy escape route for these molecules. In order for the solid to dehydrate, it has to melt before the water molecules can come out of the crystal. This is characteristic of the type of compound that undergoes hydration with melting. Very different from the magnesium stearate which is a layered hydrate.

Q. Have you prepared a demonstratives to show what it looks under the microscope when a crystalline compound melts, dehydrates, and recrystallizes?

A. This is a two images from the paper by Lin on this pharmaceutical called metrochloric, on the left we see a differential scanning calorimetry trace, on the right we have photomicrographs taken during hot stage microscopy. On the left you can see DSC and TGA traces. The DSC shows a nice endotherm that corresponds to melting and dehydration. You can tell it's melting and dehydration because this is immediately followed by an exotherm that correspond to recrystallization. At much higher temperatures the anhydrates form that's generated melts.

On the right, Lin showed on the right we have frames from Lin's figure two which showed what happens when you have a melting and dehydration followed by recrystallization. You can see here at 69 degrees centigrade the crystals are impacted, we dehydrate with melting here, so this is shown at 88 degrees in the upper right.

THE COURT: Just a moment. We're on DDX 6.45. You're pointing at the figures from DTX 99 and you said here and here. You were pointing first at the upper left hand box, then at the upper right-hand box which have the 69 degree and 86 degrees centigrade numbers in the lower left-hand corner of each of those pictures. Maybe that's 88.

THE WITNESS: It's 88.

THE COURT: Okay. Again, just helps for purposes of having to go back and read this. Go ahead.

THE WITNESS: Sorry about that. Let me be clear. So you can see dehydration with melting in the upper right-hand image that was taken at 88 degrees. In the lower left-hand image which was taken at 120 degrees, you can see what happens after this melted material recrystallizes. These crystals in the lower left-hand frame look very different from the crystals in the upper left-hand frame. That's because each of one of them has nucleated and grown from an isotropic liquid you get very different shapes in this particular phase than you do if you just have a solid-solid phase transformation. Finally that anhydrate form melts and the last frame is at 184 degrees, that's the lower left image.

Q. Dr. Hollingsworth what we're looking at the DDX 6.45 which displace figures, excerpts from figure two and figure three of the Lin article, DTX 99; am I right?

A. I think that's correct.

MR. ABRAMOWITZ: Your Honor, we offer into evidence figures two and three of DTX 99.

MR. LIEF: No objection.

THE COURT: Admitted without objection.

BY MR. ABRAMOWITZ:

Q. Now, Dr. Hollingsworth, looking at all this

dehydration mechanism literature, does this mean that you disagree with Dr. Pinal's conclusion that a melt and recrystallization occurred during rehydration?

A. I disagree with that assessment.

Q. Have you prepared demonstratives to show what happens with the crystalline structure?

A. Let's look at the next demonstrative here. This is just a schematic diagram showing the structure of the hydrate before and after loss of water. The loss of water can occur at different temperatures either by heating the sample or by evacuation of the sample to remove the water, for instance, you have a layered hydrate, and the chains are ordered in the low temperature dihydrate form, that is the chains next to each other are arranged in particular directions relative to each -- they have orientational order.

The molecules of water are removed from the interlayer spacing between these long chains, that's the dehydration event. In doing so you make a rotator phase. This is a type of mesophase in which the long chain molecules are rotating rapidly along their long axis. This material has two-dimensional order, it's not a three-dimensional crystal anymore, you'll see that in the next few slides.

Q. We have been looking here at DDX 6.46. Looking at the

dihydrate here on the left side and the rotator phase on the right side, looking at the dihydrate, Dr. Hollingsworth, is this structure the same as the structure presented in Dr. Pinal's demonstratives for hydrate?

A. I think one big difference is that in Dr. Pinal's demonstrative, he's got molecules of water in two separate planes, but in this magnesium stearate dihydrate the water molecules are in one plane and one plane only. He's also gotten vertical rectangles, vertically oriented rectangles with water molecules in between them, but there is very little chance that there is much water in between these long hydrophobic chains of magnesium stearate.

Q. Are there any analytical tools you can use to determine whether a solid is a crystal or a mesophase?

A. The most important is this powder x-ray diffraction. I got a slide that shows the instrument here. This a powder x-ray diffractor.

Q. You're looking at DDX 6.47?

A. That's correct. The diffractometer is an x-ray source and a detector and the sample is usually held in a fixed position in the center here and in the diffractor experiment you change the angles of the source and detecting, you raise them both gradually and measure intensity of the diffracted x-rays that emanate from the sample. So at each -- so that, the angle of the diffraction is called the input angle and

the output angle, that's the two phase angle, as it turns out at different angles you get constructive interference of the diffractive ways and you can see a peak in the diffraction pattern.

Q. Moving on to 6.48, what sort of data or results did powder x-ray diffractogram generate?

A. So they generate what are called diffractograms showing the intensity as a functioning of the scattering of the data.

Q. Have you provided a demonstrative in DDX 6.49 which explains what the data in these diffractograms actually means?

A. Yes, I have. So notice that there are several peaks in this diffractogram, each peak in the diffractogram actually corresponds from the fraction from a series of planes that slice through the unit cell of the sample of interest. So there is actually a do correspondence between the two theta, the scattering angle and the spacing between these planes which is called the despacing, here at 3.404 angstrom, they interconverts between those two. If you have a sharp peak in the x-ray diffraction pattern it means that you have a series of planes that exhibit long range order in that particular direction in the sample at hand.

Q. And you did prepare a demonstrative to show how this data is used to differentiate the type of solids?

A. Yes, I have. The important thing here is if you get a sharp x-ray diffraction peak, that means long range order in a particular direction. So these diffraction peaks as I said give you information about the spacing between these planes and, therefore, the size and shape of the unit itself and also about the orientation of certain molecules in the solid.

So remember there were three different classes of solids, there are crystals, mesophases and amorphous materials. So crystals show sharp peaks that exhibit long-range order in three dimensions. Mesophases have sharp peaks that correspond to long range order in either one or two dimensions. And two dimensional version is the one we're interested in here, amorphous materials give only broad features on the nearest neighbor distances.

Q. We said earlier we would come back to figures five and six of PTX 493, Braconni.

DTX 6.51, what information did figure 5 of PTX 493 is important to your opinion?

A. This is a diffractogram that Bracconi collected, actually two, and normally the scale is intensity versus two theta into the D spaces, you can read right after the graph what the D space is. For example he's focused much of his paper on the so-called rotator band. That rotator band actually tells you about the spacing between the long chains

of the stearate molecules in the layers. So at 55 degrees you can see that the spacing is about 4.2 angstroms. At a hundred degrees, the spacing is closer to 4.3 angstroms, between those long chains. This is what happens when you warm up the material with the spacing between the chain gets larger.

The other thing about this though is the peak width is much smaller at a hundred degrees than it is at 55 degrees. So 55, at 55 degrees, you have a number of differently oriented chains in the sample, and the distances between these different chains is variable. You have got some that are close, some that are a little bit further apart, so you get a broader peak than you do at a hundred degrees.

At a hundred degrees the spacing between these chains evens out and so you have one characteristic distance between the chains which is longer, this shows that you have higher symmetry. We'll get to that. And you have long range order of these evenly spaced chains over long distances in that direction in the material.

Q. Does figure six of Bracconi, PTX 493 on DDX 6.52 provide additional information about what happens to the rotator phase during heating of the sample?

A. Yes. So this is a plot generated from those sort of diffractograms that we just saw. So the plot of D spacing

as a function of temperature. The bottom line is actually just from the two diffractograms we just looked at. I'm pretty sure that's true. And the other two lines are similar measurements but without the internal sodium chloride standard, so they're slightly displaced.

But the important thing is the slope of these lines is all about the same, and they're also straight lines which shows that when you evacuate these samples, or heat the samples as in this case, you're removing water, and at different temperatures the spacing between these chains changes gradually and continuously the function temperature, basically the separation between the chains increases gradually and linearly as you increase the temperature.

This is a solid-solid process that does not involve something like melting and recrystallization. This is indicative of a smooth process and you have got several data points along the way to show that it's a gradual process.

THE COURT: Would you identify this slide?

MR. ABRAMOWITZ: This is figure 6 of PTX 493 on DDX 6.52.

THE COURT: Okay. Thank you.

BY MR. ABRAMOWITZ:

Q. If we move to DDX 6.53, have you provided sort of a summary of how this mesophase or rotator phase relates to

the dehydration process?

A. So during dehydration, you're generating a mesophase to a solid-solid phase transformation. I should say that the dehydration can occur either through heating or through desiccation by evacuating the sample or putting next to some drying agent. You go directly from the hydrated crystalline phase to a anhydrous mesophase which Bracconi identifies as a rotator phase. That's how he identifies this is through the rotator diffraction band.

The point about this, the molecules are rotating around their long axis while staying in position, that's why the shape of the solid that you get after dehydration looks the same as the shape of the solid before dehydration. We saw that in the Miller and York, very nice photomicrographs. You have long range potential ordering gives you sharp diffraction peaks, but you also get fewer diffraction peaks because the symmetry of the rotator phase is higher, at least apparently higher than the low temperature or I should say hydrated phase, the dehydrated phase.

THE COURT: I think this would be a good time to take five or ten minutes.

MR. ABRAMOWITZ: We have two slides.

THE COURT: You have two slides to go?

MR. ABRAMOWITZ: Yes.

THE COURT: Okay. Go ahead.

MR. ABRAMOWITZ: I'll be two minutes.

BY MR. ABRAMOWITZ:

Q. Demonstrative DDX 6.54, have you provided a difference between the dihydrate and anhydrate phases of magnesium stearate?

A. Yes. These are shown on the left and the right. On the left we have a column showing the characteristics of the low-symmetry hydrate phase, on the right we have a column showing the characteristic of the high-symmetry anhydrate phase. Both of these exhibit long range positional order of the chain.

One of the main differences is that in the low-symmetry hydrate phrase, the molecules are not rotating rapidly about their long axis. You have so-called long range orientational order of the chains. In the high-symmetry phase of the anhydrate, the molecules that we saw are rotating very rapidly, so you only have short range orientation order of the chains. So that shows up in the diffraction pattern in the following way.

So in the low-symmetry hydrate phase you have a variable spacing between the chains, that gives rise to numerous diffraction peaks and this diffraction pattern. In the high-symmetry phrase of the anhydrate, you got an even spacing between the chains and that gives you the single rotator band.

THE COURT: What do you mean by long range and short range in this context?

THE WITNESS: So typically by long range I mean that if you know the position of a chain, say a starting point of a chain, if you have long range you can redirect the position of the chain, let's say maybe even several hundred angstroms away from that initial chain if you just know the spacing of the structure. Okay?

As you lose correlations between either positions or orientational, orientations, then you lose those correlations between nearby molecules, they only extend over shorter distances, that has a profound effect on the diffraction pattern.

It also has a profound effect on the optical property. This is an important thing here. So when we look through the plate phase of these crystals, the low symmetry hydrate phase appears to be isotropic, the chains are oriented in certain ways so the speed of light goes through the crystals, speed of light is different in different directions, that's what we mean by isotropic.

When you dehydrate this material, the optical properties are actually isotropic within the plane, the spacing between the chains is even and it appears to be hexagonal, that's one of those uniaxial crystal classes or classes of materials in which the refractive index is the

same in all directions in the plane, so the materials appear to be isotropic in the plane.

And so I think Dr. Pinal's reading of Ertel & Carstensen and other documents is way off base because it doesn't appear that he considers that what they're talking about is what they're looking at is they look through the plane of the plate phase of these materials. It looks like it's isotropic, but in fact it's overall and isotropic because the third dimension and you're just not looking in that direction at the crystal.

Q. Dr. Hollingsworth, you were here to hear Dr. Pinal's opinions about the sharp melting point and the DSCs of Dr. Hampton indicating recrystallized solid. Can a high symmetry anhydrate rotator phase have a sharp melting phase?

A. Certainly.

Q. Based on all this information, the testing, the literature, have you come to any final opinions concerning the melting point of Zydus's magnesium stearate samples?

A. Yes, I have. I see this as actually a very straightforward case. All the literature shows and testing of the Zydus material shows that magnesium stearate does not melt at or below a temperature of 90 degrees. Instead it undergoes a solid state dehydration, if you have a solid mesophase, you got two dimensional order, not three dimensional order, do the anhydrous form melts at a much

higher temperature above 120 degrees, it does not melt at 90 degrees.

MR. ABRAMOWITZ: We have nothing further, Your Honor.

THE COURT: All right. Before we start the cross-examination we'll take a ten-minute break.

(A brief recess was taken.)

- - -

(Proceedings resumed after the break.)

THE COURT: Thanks. Please be seated. Doctor, you are still under oath, of course.

Mr. Lief, cross-examination.

MR. LIEF: If we could approach with several binders?

THE COURT: Yes. Yes, please.

(Binders handed to the Court and to the witness.)

CROSS-EXAMINATION

BY MR. LIEF:

Q. Good afternoon, Dr. Hollingsworth.

A. Good afternoon.

Q. With respect to your background, would it be fair to say that the focus of your research as between solid to solid transitions and interactions versus solid to liquid transitions, the focus of your research is solid to solid

chemistry?
A. Much of it has been, but we've also looked at solid to liquid transitions.
Q. Would it be fair to say that you primarily focused on solid to solid phase transition?
A. I'd say that's a fair statement. Right. We focus mostly on solid to solid phase transition.
Q. And when you talk about, in fact, exactly what you, quote, do for a living, isn't it the case that you would say you are in the business of single crystal X-ray diffraction?
A. Well, that's one of the things I do.
Q. You do a lot of single crystal X-ray diffraction; is that correct?
A. That's right. Many of the samples are akin to the mesophase as we've been talking about, so I don't necessarily think that all of them are three-dimensional crystals. But, yes, we do a lot of single crystal X-ray diffraction.
Q. And am I correct that you have not done any research on magnesium stearate prior to this case?
A. That's correct.
Q. And you have never studied magnesium stearate in your academic work?
A. Oh, that's correct.
Q. And you've never opined before in any litigation about

the melting point of magnesium stearate; is that correct?
A. That's certainly correct.
Q. And you've never published on magnesium stearate?
A. No. That's all correct.
Q. As a subcategory, I take it you've never published on a melting point of magnesium stearate?
A. That is also correct.
Q. And you've never published on the crystal structure of magnesium stearate; is that correct?
A. There is no crystal structure of magnesium stearate, so you're correct.
Q. Is it your, is it your position that magnesium stearate is never a crystal, ever?
A. Oh, no, it is a crystal, but you asked about the crystal structure, and there is no crystal structure. We do not have atomic coordinates for all of the atoms in the crystal, the magnesium stearate.
Q. And no one has divined that structure. Is that what you are saying?
A. Not exactly. That's correct. So we know a lot about these crystals, but not the complete structure.
Q. And you've never published on a differential scanning calorimetry of magnesium stearate; is that correct?
A. That's correct.
Q. Or an XRPD, X-ray powder diffraction of magnesium

stearate. Never published on that?
A. That's correct. We've not published on magnesium stearate.
Q. You have never personally witnessed magnesium stearate melt; is that correct?
A. I've seen videos that Dr. Sacchetti collected, and so I've seen what appears to be melting of magnesium stearate from those videos but I've not done this personally.
Q. Thank you.

And you have no personal knowledge one way or the other as to whether magnesium stearate is viscous when it melts?
A. I only have information that I gleaned from the videos that Dr. Sacchetti took and from my experience with soapy materials.
Q. Now, you don't know how viscous magnesium stearate is when it melts; is that correct?
A. No, I don't in particular know how viscous it is, no.
Q. Thank you.

You've never published on what an appropriate methodology is for determining a melting point; is that correct?
A. Well, we use appropriate methodologies in our own work, but I've never had a publication that specifies for

say a class of compounds that this particular method is the most appropriate method. But we choose the most appropriate method when we do our own research.

Q. You've never published on what the appropriate methodology is in determining the melting point of anything; is that correct?

A. Well, not specifically that thing. But as I said, we choose the most appropriate method for measuring the melting point of whatever it is we're melting, and then we report that melting point using that method. So, in fact, we choose a method that we think is the most appropriate. We don't say specifically, this is the method that one should use for a particular melting point.

Q. Well, there are articles, am I not correct, and books even on how to do melting points; is that correct?

A. That's correct. I talked about McCrone's book and Brandstatter's book today.

Q. Thank you.

Am I correct that outside of litigation, you have never consulted with the pharmaceutical industry?

A. That's not correct.

Q. That's not correct.

A. I've worked with Transform Pharmaceuticals and I think that came up in my deposition, so I advised them on certain things that had nothing to do with litigation. So I call

them part of the pharmaceutical industry. They're not a pharmaceutical company, but they dealt with pharmaceutical compounds.

Q. All right. Am I correct that you have never consulted with the pharmaceutical industry on how to perform a melting point?

A. That is correct.

Q. And you've never worked in the pharmaceutical industry at all; is that correct?

A. That's correct.

Q. In coming to your opinions in this case, am I correct that you did no search of doctoral theses?

A. I'm not sure what I looked for. I think I mentioned in my deposition that I had looked for some NMR results and that there was a doctoral dissertation that had something to do with that, but the search did not go anywhere.

Q. If we could take a look --

THE COURT: I will need to know what the acronym is.

THE WITNESS: Oh, sorry. NMR is nuclear magnetic resonance spectroscopy.

THE COURT: Thank you. Sorry to interrupt, Mr. Lief. Go ahead.

MR. LIEF: That's all right.

BY MR. LIEF:

Q. If we could look at your deposition, which is tab 1 in the first volume.

A. Sorry. I'm just going to have to move these.

Q. I would like to take you to page 66.

A. Okay.

Q. And if we could look at --

THE COURT: Page 66?

MR. LIEF: If we could look at lines 12 through 15, and it continues on, and we'll read that.

THE COURT: Hold on a minute. What tab are we at?

MR. LIEF: Tab 1, his deposition.

THE COURT: Tab 1? Thank you. Go ahead.

MR. LIEF: All right.

BY MR. LIEF:

Q. And page 66, starting at line 12, the question is: And did you do a search of any doctoral theses or anything like that?

And the answer is: I did not do a search of doctoral theses.

And you went on and you said, I think that -- I think on Google Scholar a doctoral dissertation came up and at least the reference to it. I don't think I ever saw the dissertation itself. I think it had to do with solid state NMR studies of -- I don't know if it was magnesium

stearate or other related compounds, but I never followed that up.

A. That's what I was trying to tell you. Right.

Q. So --

A. But it did come up, but I didn't follow it up.

Q. If you did not explicitly -- I don't know if that's the word, you did not specifically look for doctoral theses and do a search; is that correct?

A. No, I did not. I looked on Google Scholar and sometimes a doctoral dissertation appears on that search.

Q. In terms of the testimony and the work we saw and the prior witness, Dr. Sacchetti, you did not design those studies; is that correct?

A. That's correct.

Q. And I believe we're going to hear from another witness after you, Dr. O'Halloran. At the time you issued your opinions, you were not familiar with the work of doctor owe Hal ran at all; is that correct?

A. I don't remember about doctor owe Hal ran. I don't know if I had heard of him or not, but that was not part of my report, as far as I recall.

Q. All right. There was some testimony on direct that you had been admitted in other cases as an expert; is that correct?

A. That's correct.

Q. And I think you've been admitted at least twice in two cases in Delaware; is that correct?

A. That's correct.

Q. At least one of those cases was a case relating to melting point, wasn't it?

A. There was some discussion of melting point in the Cephalon versus -- well, several defendants, a case on Armodafinil.

Q. The Armodafinil case, yes. And, in fact, in that case, am I correct that Judge Sleet rejected your opinion?

A. I don't know that that is true. What I do know is that that case went up for appeal and that it was settled because the appellate judge disagreed with Judge Sleet on many different points. So I don't know what he said about my testimony regarding melting points.

Q. If we could take a look at tab 29 in your book. Do you see this says on the front, In Re: Armodafinil, Patent Litigation, Incorporate?

Do you see that?

A. I see that.

Q. If you could turn on the bottom, there's page numbers usually in the right-hand corner. Page 25, the bottom right-hand column.

Can I read to you, quote, the Court further notes that it reaches this conclusion despite doctor's

Hollingsworth's assertion that various polymorphic form of armodafinil produced from preparation one could have converted to form one during testing on a Kofler hot bar. See transcript, and it has pages.

And then it says, specifically, the Court finds that this contention is refuted by the fact that the instantaneous melting points of form two and the mixtures involving Form 2 and 4 could be discretely measured and recorded as data points.

Moreover, Dr. Hollingsworth's conclusion is further undermined by his own testimony that he has never used or seen a Kofler hot bar, and it goes on.

Did I read that correctly?

A. You read it correctly into the record. I'm just trying to figure out what else it says here.

Q. Is that correct, that when this opinion came out in 2013, you were testifying in this case about this Kofler hot bar equipment, but you had never seen it or used it?

A. No. As I said then, this is a museum piece. It's very difficult to get your hands on one. I've actually looked for one because I was interested in obtaining one, but it cost almost 2,000 pounds, so I was not going to go there.

Q. All right. And am I correct that in another case in Delaware, Judge Stark also rejected your opinion?

A. I'm not sure what part, or if he rejected my opinion, but he disagreed with defendants in that case.

Q. All right. If we could look at tab 26 in your book.

Do you recall testifying in Bristol-Myers Squibb company versus Mylan?

A. Yes, I do.

Q. All right. And if we could look in this opinion on page 11, the bottom sort of left-hand column of page 11.

Do you see the paragraph there, beginning Mylan's expert?

A. I see that.

Q. And it reads, Mylan's expert, Dr. Hollingsworth, testified that there is a "conflict" quote as to which of the DSC patterns -- the one in the 729 patent, showing a peak at 118 C, or the one in the '372 patent, showing a peak at about 108 to 110 C is correct. The transcript cite. Dr. Hollingsworth opined that because the '372 patent was filed after the '729 patent, one of ordinary skill in the art would expect the '372 patent to be correct. This is not persuasive.

Did I read that correctly?

A. You did, and I think it is persuasive. But he disagreed.

Q. You disagree with Judge Stark on that?

A. I actually do.

Q. Okay. To come to something else you said in your direct examination, am I correct that, in fact, the material that melts above 120 degrees C is not -- one, it's not a hydrated material; is that correct?

A. As far as I can tell, it's not a hydrated material. That's correct.

Q. All right. And I believe you said during your direct, words to the effect of, it's a completely different material, or completely different substance than the hydrated material you started with; is that correct?

A. Yes. It's no longer a hydrate, so the first endotherm had to do with dehydration, and so I think my point was about the width of that peak. Dr. Pinal had testified about the narrow width of the peak. I think he said several times that it's the same material. And so my point was it's actually not the same material. It's a very different substance. The hydrate and dehydrate are very different substances. One has water and that first endotherm has to do with loss of water. The second has to do with melting of the anhydrate. So those are different substances.

Q. And you wanted to point out that you disagreed with Dr. Pinal about that?

A. That was the point. Right.

Q. All right. And would you agree with me that the substance that goes into Zydus' product is the hydrated

material?
A. That's correct.
Q. Thank you.
Now, you had a discussion of several papers and talked about x-ray powder diffraction of samples and magnesium stearate; correct?
A. That's correct.
Q. Did you hear Dr. Sacchetti's testimony that magnesium stearate that he studied was very small, very small particles of material?
A. Yes, I did.
Q. And would you agree with me that when you take an x-ray diffraction of a powder as opposed to a formed crystal, a single crystal, you get much less information from that; correct?
A. Yes, you do.
Q. Thank you.
Now, you had some discussion about the Bracconi paper; correct?
A. That's correct.
Q. If we could take a look at Braconni, I believe it's tab 24 in your book.
This is the Bracconi paper you were discussing; correct?
THE COURT: What tab?

MR. LIEF: Tab 24.

THE COURT: 24.

THE WITNESS: That's correct.

BY MR. LIEF:

Q. Now, for instance, if we could turn to internal page 116 of this.

A. Okay.

Q. These x-ray diffractograms that were taken, am I correct these are not pictures in real time as you are ramping the temperature up; correct?

A. Let me just look. Yes, it says that the set of diffractograms, so if you go to the text right here.

Q. Yes. Left-hand side under 3.2?

A. It says figure four shows a set of diffractograms obtained by analyzing a VG sample sequentially at increasing temperature.

I think the sample was held for an hour at each temperature before they started diffractogram.

Q. So they kept it at a single temperature for an hour and then took an x-ray of it; right?

A. That's correct.

Q. Now, if you had a process that was taking place, let's hypothesize, if you had a process taking place, a dehydration and a melt and a recrystallization taking place in four, five minutes, let's say, if you waited an hour, you

wouldn't see the liquid that had formed in the intermediate time period; correct?

A. Well, I reject the hypothesis because we're at very low temperatures, but if all that happens in a short period of time, then you would see the effect after any process occurred.

Q. You would see the end result which would be the recrystallized solid at the end; right?

A. If that's what you were looking at, that's what you would see. But my point is that that's not what we're looking at.

Q. I understand that conclusion, it presumes the earlier part of it. But if you assume, or were open to the hypothesis that there is a dehydration forming a melt which forms a liquid but then it recrystallizes, in this Bracconi paper, if you wait an hour to take the x-ray, you won't get an x-ray of the liquid in the middle; right?

A. Well, liquids don't show a peak in the diffraction pattern, what you're seeing is the material that's either a mesophase or a crystal that gives you diffraction peaks. But if there are other events happening in the meantime, certainly you don't see them, but that's not what's happening here.

Q. In terms of both Dr. Hanton and Dr. Sacchetti's DSC experiments, as you go through that first endotherm, what

was the ramp rate for Dr. Hanton?

A. Ten degrees per minute.

Q. And for Dr. Sacchetti?

A. He was running his five degrees per minute.

Q. To go from 70 degrees C to let's say 90 degrees C through that area of that first endotherm, for Dr. Hanton that would take two minutes?

A. That's correct.

Q. And for Dr. Sacchetti's DSC that would take four minutes?

A. That's correct.

Q. If you waited another hour, there was some liquid in the middle there, you're not going to see it on the x-ray; right?

A. You only see liquid on the x-ray as far as I can tell at very high temperatures. But no, you wouldn't see it. It's nice to have some evidence when you make a hypothesis so this is the point here that there is no evidence so there is no point in making that hypothesis or you can entertain it, but the point is if there is no evidence, then it goes nowhere.

Q. In Bracconi, this is not sort of a paper that gives a final conclusion on the events that are taking place; correct?

A. It gives several conclusions. I don't know what you

mean by a final conclusion.

Q. Well, it leaves open the possibility of further interpretation and further work to understand what's going on; correct?

A. I think there is always further work to be done, but this has a lot of information that -- in it, and one can draw many conclusions from it.

Q. If you go to page 121 of the Bracconi article, sort of in the right-hand column, maybe starting several lines down, you see where it begins the x-ray investigation?

A. I do.

Q. It goes on, "The x-ray investigation of the product obtained by cooling and solidification of the melted sample (figure 9) has no counterpart in the literature. Apart from the three weak diffraction lines already appearing on heating in figure 3 and that remain present, the diffractogram seems to reveal two crystalized faces. Additional experiments and specific literature review would be needed to develop an interpretation, but the presented data has the merit of further emphasizing the physical-chemical complexity of the system of concern and possibly raising interest for its investigation."

Did I read that correctly?

A. You did, and I think he's right. So after you take this to a very high temperature and then cool it back down,

that's shown in figure 9, you get a diffractogram that seems to be more than one thing, I think that's what he's saying.

Q. The two things he talks about sort of above and below the melting are both crystals; right, he uses the word crystal, he says reveals two crystallized phases; right?

A. Right. So in figure nine --

Q. Thank you. That was the answer.

Did you look at any of Bracconi's subsequent papers?

A. I have looked briefly at a subsequent paper of his.

Q. And you're aware that Bracconi takes the view that even in the subsequent papers, there were limits on the present understanding of the hydration and dehydration process of magnesium stearate, are you aware of that?

A. You'll have to show that to me. I haven't read those papers carefully.

Q. You didn't look at that carefully in coming to your opinion?

A. I looked at the paper from 2003 carefully. The paper from 2005 I think was not part of my report or my opinion so I have not looked at that paper carefully.

Q. You're aware that it was 2005, and you did see that paper, sir?

A. I am aware that there is a paper, but as I have said, I have not studied it recently, the most interest and

relevant part of this work had to do with the x-ray diffraction because that's very clearly what's going on as you dehydrate this material.

Q. The 2005 paper really wasn't about x-ray diffraction, was it?

A. That's correct.

Q. It was about thermal analysis; correct?

A. That's correct.

Q. If we could take a look at that, it's tab 113 in your book. Do you have that?

A. I do.

Q. If we could look towards the end of the paper in the conclusion section which is on page 50. And if you look at the last paragraph, I can read that to you. "Commercial magnesium stearate appears as more complex material than currently believed, and the present paper has not succeeded in fully clarifying the relation between its thermal and structural properties. A systematic comparison of accurate new experimental data with values extracted from the literature has revealed the limits of our present understanding of the hydration-dehydration process of magnesium stearate."

Did I read that correctly?

A. Yes, you read that part of the paragraph correctly. That's the way science works.

Q. You agree with that?
A. Well, that there are always limits to what we can understand from any work.
Q. Now, there was some discussion about the visual evidence in the case. Do you disagree with Dr. Sacchetti's testimony that it's a viscous melt and it's hard to see?
A. What do you mean it's hard to see?
Q. Difficult to spot liquid with the eye when it's a viscous melt like magnesium stearate?
A. At higher temperatures right around 130 I think it's probably true that, it's a viscous melt, and it's hard to tell exactly when the melting occurs in that case. I think Miller and York reported the same sort of thing.
Q. I want you to look a little bit at Miller and York, because you were not present when Miller and York did their experiments, take it?
A. Of course not.
Q. And I take it you don't know exactly the physical setup of their study of anisotropy?
A. I know a lot about it.
Q. You were there?
A. I didn't say that, I said I wasn't there, but I said I know a lot about it, because they describe it.
Q. And you looked at the pictures that they did pick; correct?

A. That's correct, and I read the text.
Q. And in fact, even in those pictures, even with that viscous melting liquid, am I right that there was some changes between 88 degrees and 96 degrees?
A. I don't know what you mean by with that viscous melting liquid because that's not what was happening between 88 and 96 degrees. I think you're misleading the Court if you say that.
Q. I don't want to mislead anyone. Let's take that out of the question, but I don't think so.
A. Could we go to the images.
Q. We're going. Between 88 and 96 degrees, there was some changes, I think you even said it on direct, there were some changes in what those crystals looked like?
A. Yeah, there were some striations in the crystals that you could see at 96 degrees. The dehydration occurs with the water leaving from the edges of the crystals, so the edges were straight, but there was strain that developed along the edges and I think you can see the striations developing along the edges of the crystals as well. But the edges were straight, so it's very clear that the material retained its shape during this process.
Q. Did you look at the pictures really closely?
A. I did.
Q. And it's your testimony that there weren't at least a

few features that just disappeared as you went from 88 to 96?

A. I think you need to show it to me because --

Q. Why don't we take a look. It's tab 28 in your book. We have blown up some of the sections of these pictures and we have zoomed in on a little shape there. Can you see --

A. Sorry. Hang on.

Q. I'm sorry.

A. Which tab? 26?

Q. All right. What this is, tab 28, is from Miller and York, and it's from the same figure that you were looking at with the pictures of the various temperatures. Do you recall these pictures during your direct?

A. Yeah, those were the first two frames that I looked at and that we showed in my direct. I'm sorry, I got the wrong binder here.

Give me one second. You have a lot of stuff up here.

THE COURT: It's in two of three. It's in number two of three.

THE WITNESS: Right.

Q. Can you see that. Do you have it?

A. I see it.

Q. And am I correct that on the left-hand side we have a blue arrow that's pointing to what I'll describe as the corner of a crystal, and in the right-hand side at 96

degrees the corner of that crystal has disappeared?
A. I don't know if we're looking at the corner of a crystal or a ledge on that crystal, but it's not really clear to me what exactly that represents. But there is a difference in appearance between those two frames.
Q. Thank you.
When you say it's not clear what it represents, that's because it's difficult to look at these visual images and know what you're looking at; right?
A. I think they do contain a lot of information. I don't know about difficult to look at them and know what you're looking at. You can very clearly see that the edges of this material are straight, and that's where the water is leaving the crystal.
Q. Can you see the water leaving the crystal in these pictures?
A. Of course not.
Q. But I think you would agree with me that somewhere around 88, 90 degrees, I think we all agree, there is certainly a dehydration occurring?
A. That's right.
Q. But you can't see it, can you?
A. Sorry?
Q. You can't see it?
A. I wasn't finished. I started to say that the water

molecules leave the crystals from the layers and so the layers open up on to the top and right and left edges of the crystal. The water is not going to be coming through the plate phase because it would have to travel through these long chain.

Q. Wherever it's coming from, do you see little bubbles of water anywhere?

A. No, you would have to put the crystal under silicone oil to see bubbles of water coming off.

Q. So this doesn't show something that despite the fact that it doesn't show it, you know it's occurring; isn't that right?

A. Well, certainly I think that at this temperature water has a very high vapor pressure and it's probably gone as soon as it leaves the crystal.

Q. Now, magnesium stearate, to use sort of a very general chemical term, is a fatty substance; right?

A. I think that's a fair assessment of what it is.

Q. All right.

A. Yes.

Q. With that in mind, you spoke about McCrone. McCrone is an authoritative author; is that correct?

A. I would say so, that's right.

Q. And you would respect his views of things; is that correct?

A. Yes. We talked about this very thing at my deposition, as I recall.

Q. All right. If we could look at McCrone, I think we have it in your book at tab 39.

This is one of the references that you rely on; is that correct?

A. That's correct.

Q. And if we could go to page 53 in McCrone. At the bottom there's a paragraph that begins, occasionally.

Do you see that?

A. I see that.

Q. And it reads, from McCrone, occasionally, it is necessary to observe melting points on complex mixtures, such as waxes, fats, and oils. Such materials melt over a wide range as successively higher melting eutectics become liquid. Subtle polymorphic transformations often also take place. Because the eye is not particularly sensitive to subtle changes taking place slowly over a period of several minutes, it is advisable in many of these cases to replace visual observation, it goes onto the next page, to replace visual observation with an instrumental means of recording such changes.

Did I read that correctly?

A. Yes, and that's what Dr. Sacchetti did. His instrumental method was a video camera.

Q. Well, when McCrone wrote this, there weren't iPhones with video cameras on them; right?
A. Well, he used a photocell.
Q. DSC is an instrumental method; right?
A. Sure, it is.
Q. Okay. And you don't disagree with McCrone, or maybe you do, that these kinds of fats are difficult to observe melting?
A. Yes, and so temperatures run 130 degrees. I think it's difficult to tell exactly where the melting point is.
Q. But -- strike that.

To kind of take on a different point, if we could -- you would refer to pictures from a microscope, pictures from a microscope as showing macroscopic shape; is that correct?
A. Sure. I think that's probably fair.
Q. And, in fact, you did that in your expert report; is that right?
A. Did what?
Q. You referred to microscope pictures as showing a macroscopic shape?
A. Yes. I would say that macroscopic means having to do with large ensembles of molecules. We have not defined the exact limits between microscopic and macroscopic, but I think that's fair.

Q. All right. Turn to a different topic.

Liquids, I think you would agree with me, liquids simply do not have anisotropy at all; is that right?

A. Liquids are isotropic.

Q. All right?

A. That's correct. That's part of the definition of a liquid.

Q. All right. And crystals are anisotropic; is that correct?

A. Most are. Cubic crystals are not.

Q. Cubic crystals are not. Magnesium stearate isn't a cubic crystal?

A. No. At high temperature it appears to be a hexagonal mesophase which exhibits anisotropic in certain directions, but not others.

Q. Well, Dr. Hollingsworth, let's go through it. The hydrated form of magnesium stearate is not a cubic crystal; is that correct?

A. Certainly correct.

Q. It's not a uniaxial crystal; is that correct?

A. As far as I can tell, that's true.

Q. And it's not anything you would call an isotropic crystal; is that correct?

A. That's correct.

Q. Okay. And with respect to the dehydrated form of

magnesium stearate, the truth is that the symmetry of that phase is still not known; is that correct?

A. That's correct.

Q. Thank you.

A. But the optical properties of that crystal appear to approximate that of a hexagonal or uniaxial phase.

Q. What were your words? Appear to approximate?

A. Appear to approximate --

Q. Thank you.

A. -- that of a uniaxial or hexagonal phase.

Q. Now, those words -- strike that.

With respect to the Miller and York article, the Ertel and Carstensen article and also the Rajala-Lane article that you spoke about, am I correct that every one of those articles reports the loss of anisotropy in association with dehydration; is that correct?

A. They all do so, and the only interpretation of that that I can see that's viable is because they are looking at the plate face of these samples, the samples appear to be isotropic because they are uniaxial.

Q. That's your interpretation; is that correct?

A. That's not just my interpretation. It has to do with the interpretation of Bracconi who looked at the powder X-ray diffraction pattern of these materials and discusses at length that they appear to be at least close to

hexagonal. He cites earlier literature.

Ertel and Carstensen actually cite Vold when they state that the material appears to -- well, loses anisotropy or loses three-dimensional lattice structure.

And so this all makes sense if you understand that uniaxial materials look isotropic when you look down unique axis, which is what we're doing, certainly in Miller and York's experiments. That's that photomicrograph that we have.

Q. Is it your testimony that when these three authors said there's a loss of anisotropy, somehow they missed it and the anisotropy was still there?

A. Oh, they are looking down through the layer and, yes, that is my testimony, that they are missing anisotropy because they're looking along the unique axis of a hexagonal or what appears to be at least close to a hexagonal mesophase.

There's just no question about it in my mind. This is exactly the sort of thing that we saw at minus 175 degrees in the crystals. As you raise the temperature to the stage transition, it goes from a low symmetry crystal to a high symmetry form and it loses anisotropy in the plane, the AB plane of the material. This is a common occurrence that goes throughout the literature.

Q. That statement does not appear anywhere in those three

articles, Miller-York, Ertel-Carstensen or Rajala and Lane; is that correct? That's your statement, not theirs?

A. But they never say that the crystals regain anisotropy. They say it loses anisotropy. And what we know from Bracconi and other papers is that the crystal turns into a two-dimensional mesophase that has high symmetry.

This all makes sense if you understand that. And I think that Dr. Pinal just simply did not understand that. He couldn't tell the Court what the optical properties of a hexagonal crystal were. But these people knew that.

Q. Dr. Hollingsworth, the answer to my question is, that for all of those articles, what they say is there was a loss of anisotropy. They don't say in one direction as to another. They just say a loss of anisotropy; right?

A. They are telling you what they observed.

Q. Thank you.

Now, to turn to a different subject, there has been some discussion about the onset and whether that is, you know, what that means in terms of melting.

Do you know what kind of differential scanning calorimetry machine Dr. Sacchetti used?

A. I'm not sure. I didn't look at the brand.

Q. Okay. I take it you also did not look at the manufacturer's guidance on how to use the machine?

A. I -- I don't know if I have seen that or not. I think it depends on the instrument manufacturer. I've seen lots of those sorts of things.

Q. Okay. If we could take a look at, I think it's tab 13 in your book, which I believe is Dr. Sacchetti's report. And I'd like to look at page 4, paragraph 14.

A. Sorry. Tab 13?

Q. You can see it on the screen.

A. Well --

Q. This is not a long issue.

Do you see in his section on DSC testing, he says he uses a TA Instruments Q2000 DSC?

Do you see that?

A. I see that.

Q. All right. And did you know about that at one point in time?

A. Know about what?

Q. That this was the machine he used.

A. I've seen his report, so I certainly have read that, but I didn't remember exactly.

Q. All right. And I take it though you did not look at TA Instruments' manual on how to use the machine in coming to your opinions here?

A. No. I might have seen that manual before, but it's certainly not incumbent in my opinion.

Q. All right. If we could look at it, it is -- I believe it is tab 79 in your book.

Have you ever seen this?

A. I don't know if I have or not. I've seen lots of manuals.

Q. All right. And if we could take a look maybe at page 50. And you see there, this is the section on temperature calibration.

A. Okay.

Q. Do you see that?

A. Right.

Q. And it reads in the second sentence there, the extrapolated onset of the recorded melting point of this standard is compared to the known melting point, and it goes on.

Did I read that correctly?

A. Yes, and so they are talking about indium and, in fact, that's what you do when you study indium.

Q. That's how you calibrate the machine; right?

A. That's right. The temperature that you use for indium is widely regarded as the onset temperature, so that's what people use, and so you calibrate accordingly.

Q. All right. And the fact of the matter is, many, many scientists view that onset temperature as the equilibrium temperature; is that correct?

A. I'm not sure that that is the case.
Q. Have you looked into that in the literature?
A. Are you talking about indium or in general?
Q. In general. Beyond indium.
A. Well, as I said in my deposition, I think this depends on the sample. So in some cases, it works. In other cases, it doesn't. And in some cases, you look at the maximum. In other cases, you look at the onset. It all depends on how sharp the melting point is. And so there's a wide literature on that. And, yes, I have looked into that.
Q. Okay. And I take it you're aware that there are articles that talk about the extrapolated onset as being pretty good measure of the equilibrium melting temperature; is that correct?
A. I think there are lots of caveats that you would have to place on that and that depends on the heating rate and all sorts of other things, and especially the type of material. In certain materials, it's a pretty good approximation. In many others, it's not. I think it depends on the type of material.
Q. So, for instance, if we could take a look at tab 103 in your book. And you see this is an article in the "Journal of Thermal Analysis and Calorimetry," Volume 78, from 2004, pages 7 to 31.
Do you see that?

A. Okay. I see that.

Q. All right. And it's published by someone named Bernard Wunderlich?

Do you see that?

A. I see that.

Q. If we could turn to page 15 in this article. Towards the bottom of the first full paragraph, about three lines up from the bottom, do you see there's a sentence that reads, the extrapolated onset of melting is a good approximation of the equilibrium melting temperature?

Do you see that?

A. Well, it says that, but this figure refers to DSC trace sharply melting standard, so I think we have to take this into context.

As I said, different materials. With different materials, you use different information. I think the USP tries to push you towards getting agreement between hot stage microscopy and DSC, and the most appropriate melting point is the one that coincides most closely with hot stage microscopy. That is in the 1995 USP.

Q. And the USP also says that instrument methods have largely supplanted visual methods; is that correct?

A. I don't remember that statement exactly. I think that you are probably right that it says that, but I'm talking about the part of the USP that states that neither the onset

nor the maximum is necessary as a melting point, and that you should seek correspondence with the hot stage microscopy experiments.

Q. All right. Move to a different topic.

Dr. Hollingsworth, am I correct that it is a known phenomenon that you can have a melt of material followed by a fast recrystallization of that melt. There are materials that do that; is that correct?

A. There are some materials that do that. That's true.

Q. Okay. And so, for instance, if we could quickly take a look at tab 104 in your book. If we could quickly take a look at tab 104 in your book, and you see this is an article from the journal polymer?

A. Okay. I see that.

Q. And it's by an author Androsch, volume 55, 2014, page 4932, do you see that?

A. Yes.

Q. If we could turn to page 4940, in the conclusion section, do you see there in the third paragraph down, left-hand side that begins reorganization?

A. Okay. I see that.

Q. And it reads, reorganization of alpha prime crystals follows a qualitatively different pathway at temperatures higher than 145 degrees C. At temperatures near the zero

entropy production melting temperature of the initially formed alpha prime crystals, stabilization/perfection of alpha prime crystals does not proceed via solid-solid crystal reorganization, but complete melting within few hundreds of milliseconds followed by fast recrystallization of the melt at the same temperature.

Did I read that correctly?

THE COURT: Actually not. You said solid-solid instead of solid state, Mr. Lief.

MR. LIEF: I apologize.

THE COURT: Don't feel like you have to read the whole thing again.

MR. LIEF: That's fine.

BY MR. LIEF:

Q. Other than that, solid state, did I read that correctly?

A. Yes, it looks like the authors used very rapid DSC and other techniques to look for this and evidently they found some very fast recrystallization.

Q. It's possible for something to melt and then recrystallize in milliseconds; right?

A. Yes. And it's possible to have a solid phase transformation that happens in milliseconds or even faster.

Q. All right.

A. That doesn't mean it's happening here, it's just a

possibility. There is no evidence in this case that this is happening.

Q. You spoke about -- you spoke about exotherms not being present; right?

A. I think I showed you several DSCs where there was absolute no evidence for an exotherm, that is correct.

Q. It is a known phenomenon that when you have multiple events taking place around the same temperature, you can get an exotherm buried in an endotherm; correct?

A. It is possible, but no one has ever found that in particular instance. It certainly would have been possible for plaintiffs to look for that by using modulated DSC or very slow warming rates, but they didn't try.

Q. All right. Now, it is possible to have that exotherm buried in an endotherm; correct?

A. Yeah, there are all sorts of events that happened under these endotherms.

Q. If we could have you quickly take a look at tab 32 in your book. You see this is from a book called liquid crystals two, it's have a book called recent developments in polymer research, Anthony V. Hopper, do you see that?

A. Yes, I see that.

Q. All right. And if you look in the segment we have, it's have chapter three, multiple melting behavior, do you see that?

A. Right, I see that.

Q. All right. I would like to take you to page 63, the top. Do you see the sentence that begins when endothermic and exothermic events?

A. I see that, yeah.

Q. And it reads, "When endothermic and exothermic events take place simultaneously, standard DSC reveals only the net excess heat flow rate, i.e., in figure one, the recrystallization exotherms in correspondence of peaks one, two and four are hidden by the simultaneous more intense melting."

Did I read that correctly?

A. You did as far as I can tell, and that's why I think the plaintiffs could have used modulated DSC which is the technique that these authors used to uncover that, they wanted to know what was going on, they could have tried that.

Q. There's a phenomenon that does occur with an exotherm for a recrystallization buried in a melting endotherm, right?

A. Certainly it is possible, I have never seen any evidence in this particular case that it's happened with magnesium stearate.

Q. And, in fact, Giron, one of the authors, Giron, one of the authors that you referred to in a different article from

which you referred, to describes this same phenomenon; right?

A. I think I have seen that article in which he shows that by using different heating rates that you can uncover processes that are all folded into one endotherm peak.

Q. Now, it's your position that there is no recrystallization occurring from magnesium stearate anywhere around that first dehydration endotherm?

A. That's correct. This is not the kind of compound that would do that. I showed you some examples of compounds where that sort of thing happens.

Q. And no reasonable scientist would say a thing like that; right?

A. Say what?

Q. No reasonable scientist would say there is recrystallization occurring associated with that first endotherm for magnesium stearate?

A. As I said at my deposition, no reasonable scientist would make that conclusion without any evidence to support that conclusion.

Q. And you cited to the Sharpe paper, that's a -- he's a reasonable scientist that you're willing to cite to his paper; correct?

A. Yeah, I think that there are reasonable -- certainly Brittain and Newman I know. I don't know Sharpe.

Q. And Brittain is a reasonable scientist in your view?
A. As far as I can tell.
Q. Were you aware that the Sharpe paper, in fact, was a piece of work that came out of Stefan Sharpe's Ph.D. thesis, were you aware of that?
A. No, I wasn't.
Q. I take it you didn't look at his thesis?
A. No.
Q. Were you aware that Dr. Harry Brittain approved his thesis?
A. No, I have no information about that whatsoever.
Q. Why don't we take a look at tab 61 in your book. If we could look at the second page in, do you see that this is titled physical and chemical properties of the pseudo polymorphs of magnesium stearate and magnesium palmitate related to their lubricant efficacy by Stefan Sharpe, do you see that?
A. I see that.
Q. If you look at the signatures of people who approved this at Rutgers University, do you see the third signature is Harry Brittain?
A. Yes, I see that.
Q. I would like to take you to page 85 of the thesis and if you look at the bottom of the page, do you see the last sentence there, it reads, do you see it, it reads, "The

equivalence of this temperature with that observed for the anhydrate phase indicates that the dihydrate phase recrystallizes to the anhydrate phase upon dehydration."

Did I read that correctly?

A. You read it correctly, but I certainly disagree.

Q. Thank you. You disagree with Dr. Sharpe now?

A. I disagree that this recrystallization, you don't make a crystal at high temperature, it's mesophase, it's not a crystal, it's mesophase.

Q. Dr. Sharpe said it was a recrystallization?

A. He's wrong about that.

Q. Page 87, if we could go to that, at the top, same kind of statement again, second line in. "The equivalents of this temperature with that observed for the anhydrate phase indicates that the dihydrate phase recrystallizes to the anhydrate phase upon dehydration."

Did I read that correctly?

A. Yes. I'm just say that Brittain's chapter in his own book talks about the different methods, I'm sorry, different mechanisms of dehydration. Several of those involve solid to solid conversions that are described as recrystallizations, even though a melt never occurs, so those are Galwey's mechanisms of one through four or so, and so recrystallized does not necessarily mean that you go through a melt or a solution phase, you can go from one

crystal form to another just as I showed at minus 175 degrees when you go from an orthorhombic phase crystal sample to a single trig, that's a recrystallization if ever there was one. He's wrong about this recrystallizing, it doesn't make a crystal, it makes a mesophase, but I'm not going to read into that that he means that this goes through a melt, it does not.

Q. Well, the classic definition of crystallization and recrystallization is, in fact, going either through a melt or a solution; correct?

A. I don't think that's accurate.

Q. You don't think that's accurate?

A. That's one way that people -- that's a common way of making crystals through -- from a melt or from a solution, but in fact modern literature shows very clearly that during phase transitions that are solid-solid, solid-solid phase transitions you can get what is effectively a recrystallization, and you see that in my photomicrographs.

Q. If we could look at tab 30 in your book. Chambers Science and Technology Dictionary, you have heard of that?

A. I have heard of it, yes.

Q. All right. And if you look at page, the first page in, right-hand column there, it's page 216, there is a definition of crystallization, do you see that? It says, "Slow formation of a crystal from melt or solution." Did I

read that correctly?
A. You have read it correctly, but I don't think that's the comprehensive definition that I would accept.
Q. You don't accept that either?
A. Pardon.
Q. You don't accept that?
A. No, you can crystalize something from another solid such as amorphous phases, amorphous phases are solid, they can crystallize.
Q. In preparing your opinion in this case, you found no literature, am I correct, and you know of no literature that describes the dehydration of magnesium stearate as causing a melt; is that right?
A. That's correct, as far as I can tell.
Q. And so that didn't form any part of your opinion because you didn't see any literature like that; right?
A. I saw lots of literature that indicate that this is a solid-solid phase transformation, so yeah, I didn't see any credible evidence that there is a melt involved.
Q. If you take a look at tab 59 of your book, do you see that this is an article from Pharmaceutical Development and Technology from volume ten, page 423 in the year 2005. Do you see that?
A. I see that.
Q. You have heard of the Journal of Pharmaceutical

Development and Technology?

A. Probably, yeah.

Q. And the title is Impact of Solid State Properties on Lubrication Efficacy of Magnesium Stearate, do you see that?

A. I see that.

Q. The first author is Rao, R-A-O?

A. I see that.

Q. I would like to turn you to page 433. Left-hand column.

MR. ABRAMOWITZ: What tab are you on?

MR. LIEF: This is tab 59.

BY MR. LIEF:

Q. Tab 59. Left-hand column about halfway into the first paragraph, do you see where it says the prominent peak in sample three?

A. Where are we?

Q. We're highlighting for you. It says, "The prominent peak in sample three shows both dehydration and melting. A close observation of this peak, (figure 6C) revealed that it starts with a small hump indicating the dehydration of tightly bound water at 82 degrees C followed by simultaneous dehydration and melting. Single broad endotherm in sample four (figure 6D) indicated merging of dehydration and melting events."

Did I read that correctly?

A. Yeah. When you look at figure 6C --
Q. Thank you, Dr. Hollingsworth.
Now, Dr. Hollingsworth, am I correct that in some respects in your testimony, you have exhibited a bias for finding solid to solid transitions where in fact there is a recrystallization from a melt, you have done that in court, haven't you?
MR. ABRAMOWITZ: Objection. Argumentative.
THE WITNESS: I'm not sure what you're talking about.
THE COURT: You got to let me rule.
Overruled. Go ahead.
THE WITNESS: As I said, I'm not sure what you're talking about.
Q. Did you give testimony in Canada in a patent case involving Abbott Laboratories and Pharmascience, Inc.?
A. I think that's true, yes.
Q. And you were on behalf of Pharmascience, Inc.; isn't that right?
A. That's correct.
Q. And if you could turn to what is tab 21 in your book, this is the report from the Canadian case. Do you see on page 15 it list you as one of the experts, Dr. Mark V. Hollingsworth, an associate professor of chemistry at Kansas

State University?

A. I see that.

Q. And if you go to page 27 of the reported case, do you see at the bottom of page 27, it summarizes your opinion in that case, and it says Dr. Hollingsworth summarizes his opinion in the following terms. Abbott's process for the preparation of form two clarithromycin requires recrystallization of clarithromycin to provide form two. And then going on to the next page underneath the furthermore in that paragraph, A, you state according to my own experimental studies that process involves a solid-solid transformation from form zero to form two and that is facilitated by water. Do you see that?

A. That's correct.

Q. And your testimony there was that there is a solid to solid transformation; correct?

A. That's correct, and I have shown that sequence of images to many, many people.

Q. If we go to page 50, the court's conclusion, at the bottom, last paragraph, "While much was made by counsel for Pharmascience of evidence presented by one of its experts as to testing that he had carried out in an effort to demonstrate the solid state or solid to solid transformation theory, I am satisfied that the responsive evidence relating to that testing, the cross-examination of Pharmascience's

expert with regard to that testing and the responsive testing of Dr. Chyall are sufficient to support the conclusion that the alleged solid state or solid to solid transformation is much more likely to be a solution mediated crystallization or recrystallization." Did I read that correctly?

A. You read it and I absolutely disagreed with that finding.

Q. You disagreed with that court?

A. Completely.

Q. One last thing. You're aware that this very issue of the melting point of magnesium stearate was tried in the Southern District of Florida?

A. I am.

Q. And you're aware that actually Dr. Pinal, our expert, testified on behalf of us that it melts below 90 degrees?

A. Yes, I understand there is a different claim construction for melting in that particular case.

Q. And, in fact, Dr. Harry Brittain testified on the other side; isn't that right?

A. That's my understanding.

Q. And you understand that the court found that -- well, why don't we look at it. Can we bring up the Florida opinion from 2013. If we could look at page 20 of Judge Middlebrook's opinion?

A. Can we tell me --
Q. I'm afraid this we don't have in the book, I apologize. If we look, have you looked at this in coming to your opinions, did you look at the opinion from Judge Middlebrook?
A. Not that I know of, no.
Q. All right. And it concludes there saying, Considering the different expert opinions and the evidence presented, I find that plaintiffs have proven by a preponderance of the evidence that magnesium stearate dihydrate -- the substance used in the Watson ANDA product -- melts below 90 degrees C. In making this determination, I found Dr. Pinal's analysis very credible.

Did I read that correctly?

A. You read it correctly. That's correct.

MR. LIEF: No further questions.

MR. ABRAMOWITZ: Do you have a copy of that opinion? Has that been provided to us?

THE COURT: Hold on. If you want to confer with him off the record, that's fine, but you can't have counsel to counsel conversation on the record. All right, Mr. Abramowitz? Either speak through me, or if you want to have a moment to confer with him off the record, I will let you do that.

MR. ABRAMOWITZ: Your Honor, we move to strike.

They did not provide the Court nor us with a copy of that opinion.

THE COURT: Yes. Well, I'm not striking the testimony. You've got access to that opinion. If you want to redirect him, it would have been the better practice to have it available, but it's not worthy of striking the testimony.

Go ahead. Get on with your redirect, please. Actually, let me ask you a question: How long do you believe you'll be taking?

MR. ABRAMOWITZ: Ten minutes.

THE COURT: Okay. Let's go for ten minutes.

REDIRECT EXAMINATION

BY MR. ABRAMOWITZ:

Q. Dr. Hollingsworth, Mr. Lief has talked to you about a number of cases where you've testified in Delaware and other places. Have you ever been excluded on Daubert or similar grounds?

A. No.

Q. To the extent you're aware, have you ever been found not credible?

A. No.

Q. If we go to Exhibit 121 in the cross binders, the other Bracconi paper. It should be 113.

A. Say it again.

Q. I believe it's 113.
A. Okay.
Q. Do you recall being cut off by Mr. Lief when you were trying to answer with respect to your understanding of Figure 9?
A. Sorry. Are we on the right page? You said tab 113? I think there's, the original Bracconi paper must be at a different tab. You've got me at a 2005 paper.
Q. Why don't we look -- if you look at page 44, and in the left-hand column, starting with the sentence that starts with "at increasing" in the first paragraph says, Bracconi, et al provides some opinions regarding the hydrating and melting theory?
A. Yes. They say that at increasing temperature under dry gas flow, all investigative materials, one or more several successive exothermic weight losses up to approximately 100 to 210 degrees Centigrade and one then one of four thermal events. That must be a typo because they mean endothermic there.
Q. If you could go to Exhibit 59, the Rao paper. Excuse me. Mr. Lief cut you off when you were testifying about, on page 431, about the samples known as Sample 3 of magnesium stearate, and Figure B.
Could you provide the rest of your testimony on Figure B?

A. I'm sorry. I thought we were talking about Figure 6C.
Q. Oh, sorry. Excuse me. 6C. Yes.
A. Yes. So the thing about that endotherm is that there's just one single endotherm for this particular sample. There are no separate endotherms for dehydration of melting, and so they're talking about merging of melting and dehydration in that particular case because there's only one endotherm in the DSC. It's clearly shown here.
Q. And --
A. And both happened because they can see it melting and it also loses water.
Q. And if we look at Figure 6B, they provide another theory that talks about the overlap of melting and dehydration.

Do you see that?

A. That's right. Those two endotherms are overlapped in that DSC trace.
Q. But the first endotherm is the dehydration endotherm.
A. It looks like --

MR. LIEF: Objection. Leading.

BY MR. ABRAMOWITZ:

Q. What's your understanding of the first one?
A. Yes. So they label it as loss of water, and then there's a point right between these where they say, overlap of melting and dehydration, and it looks like it's followed

by a melting endotherm.

Q. So is the melting and dehydration in the second endotherm of the process?

A. Well, they say that melt and dehydration are overlapped. It looks like the second endotherm is a melting endotherm and the first endotherm is a dehydration endotherm, but they overlap in this particular sample. There's no separation between them as in the DSC that we've seen in the present case.

Q. Earlier you were shown a Sharpe thesis. Do you recall that?

A. That's right.

Q. And there were some conclusions about recrystallization.

Do you recall that?

A. That's correct.

Q. Did these conclusions make it into the peer-reviewed publication that Sharpe offered?

A. Not that I know of. Actually, I'm pretty sure they did not.

Q. Going to the Sharpe thesis, which is tab 61, can you read into the record Dr. Sharpe's conclusions on page 87 about the DSC results for the commercial magnesium stearate?

A. So at the bottom of the page under that head, it says,

the commercial lots from Mallinckrodt SLC 50, SLC 51 and SLC 52 all exhibited comparable thermal behavior, Table 4.4. And so see two thermal events: A lower one that occurred at 106 to 112 degrees Centigrade, then along with the TG findings may be indicative of dehydration of a material and a higher thermal event that occurred at 122 to 123 degrees Centigrade, which seems to represent the melt of the anhydrate phase of the materials.

Q. And if you look at the next two paragraphs, is that -- are those conclusions repeated? There are two batches of commercial material.

A. Yes. On the next paragraph, they talk about a lower endotherm that occurred at 79 to 83 along with TG may be indicative of dehydration and a higher thermal event at 141 to 142, which also seemed to represent the melt of the anhydrate phase.

And down below they talked about similar things. They say, these thermal events occurred at comparable temperatures for all three lots and range from 68 to 142. So, yes. It looks like they're just saying the same thing.

Q. And the recrystallization question that Mr. Lief asked you, were those recrystallization questions all describing phenomena in the purified form of magnesium stearate?

MR. LIEF: Objection. Leading.

THE COURT: Overruled. Answer if you can.

THE WITNESS: I'm not sure exactly which samples he was referring to when he talked about recrystallization. If you take me to the page, we can look into it more carefully. There was one on page 87.

BY MR. ABRAMOWITZ:

Q. That's correct.

A. Wait. That might not be the one, because that's about magnesium palmitate.

Q. And to correct, on page 87 and 86, that recrystallization, is it describing magnesium stearate or magnesium palmitate?

A. It's describing, describing magnesium palmitate dihydrate there.

MR. ABRAMOWITZ: We have no further questions.

THE COURT: All right. Thanks very much, Dr. Hollingsworth.

THE WITNESS: Sure.

THE COURT: You may step down. Thank you, sir.

(Witness excused.)

THE COURT: Let's take a moment to talk about where we stand logistically here. What's your plan for tomorrow? Mr. Gaertner?

MR. GAERTNER: We expect to wrap up the

infringement case, Your Honor, and defendants will not be presenting any invalidity defense, so we expect to close tomorrow.

THE COURT: All right. So you'll be -- so you do not expect to be presenting invalidity you said and you will be finishing up tomorrow?

MR. GAERTNER: Yes, Your Honor.

THE COURT: All right. Good.

I don't want to say you may if you really feel like you want to make closing arguments, but this is a bench trial and there's going to be a lot of opportunity for preparing proposed findings of fact and conclusions of law. Right?

MR. GAERTNER: I would agree.

THE COURT: So I would prefer to have you submit your findings and conclusions and have -- and I will also give you some briefing in which you can make argument associated with those findings and conclusions.

Do you feel like you're going to need -- I hear Mr. Gaertner he does not feel like he needs a closing argument. Do you need something, Mr. Haug?

MR. HAUG: No, Your Honor. Well, I think whether we have a closing argument is entirely up to Your Honor, if that would be helpful. I'm fine with doing post-trial findings, brief, and if you think it would be

helpful to the Court, I would be happy to do that.

THE COURT: I just think the most helpful thing is going to be for you folks to put it on paper and give it to me. Right?

MR. HAUG: Correct.

THE COURT: Because I'm going to have to prepare my own decision. I will have to look at what you all say. By the time you get the written materials to me, I expect some time will have passed. So the impact of the eloquence I'm sure I would hear on both sides will have been lost by then.

It's probably going to be -- and I'm not trying to be a wise guy, I'm sure you'll both do a wonderful job in closing. I just don't think it would be particularly helpful because I am going to want written submissions. I think the written paper will be more effective.

So I would plan that what we'll do is, we'll hear the rest of the defense case on infringement. We'll have some rebuttal case or not from you, Mr. Haug?

MR. HAUG: If we do, it won't be all that much, and I don't think we have a lot of time left either.

MR. GAERTNER: And --

MR. HAUG: We'll certainly finish tomorrow I'm pretty sure.

MR. GAERTNER: I do have an issue about that,

because Mr. Haug did suggest that he was going to put on two witnesses for rebuttal, Dr. Pinal and Dr. Sinko --

MR. HAUG: Are you finished?

MR. GAERTNER: Okay.

MR. HAUG: I was obligated to tell the other side whether we would call anyone, so that's what we did according to our procedure. But your case isn't finished, and I just heard now that they are not even putting in an invalidity case. I was not aware of that.

THE COURT: So now you've heard they're not doing an invalidity case. That may change what you do. If you think you need to put somebody on the stand, you know, I will let you two work it out. If you feel like there's something more or in addition that needs to be said from witnesses that are here and available, you guys figure it out. Okay?

But what I'm hearing is, we're wrapping up tomorrow. I think that's great. And I look forward to seeing everybody here tomorrow morning at 9:00 a.m. Thanks very much.

(Counsel respond, "Thank you, your Honor.")

(Court adjourned at 4:54 p.m.)

I hereby certify the foregoing is a true and accurate transcript from the court reporters' stenographic notes in the proceeding.

/s/ Brian P. Gaffigan
Official Court Reporter
U.S. District Court